



An integrated modelling framework for risk management optimization, combining Effect-Based-Monitoring, Quantitative Microbial Risk Assessment and Quantitative Chemical Risk Assessment

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Abstract

Deliverable D4.3 presents an integrated risk assessment framework that combines Quantitative Microbial Risk Assessment (QMRA), Quantitative Chemical Risk Assessment (QCRA), and Effect-Based Monitoring (EBM) to support evidence-based, health-oriented decision-making in drinking water management.

The framework harmonizes microbial, chemical, and effect-based lines of evidence within a unified, probabilistic structure, enabling consistent comparison of acute and chronic health risks for different disinfection and pre-treatment scenarios. The report describes the methodological development of the framework and its application to three case studies — Berlin (Germany), Western Ukraine, and Milan (Italy) — which represent diverse hydrogeological contexts, treatment configurations, and data availability conditions.

Across the three sites, the framework demonstrates its flexibility and scalability: it integrates high-resolution microbial data from ultrafiltration enrichment to evaluate the influence of riverbank filtration for microbial risk control (Berlin), combines QMRA and QCRA to evaluate riverbank filtration and post-chlorination performance (Ukraine), and fully merges QMRA, QCRA, and EBM to support advanced treatment optimization (Milan).

Results show that (i) subsurface barriers can provide substantial log-reduction capacity but exhibit pathogen-specific variability; (ii) disinfection remains essential for microbiological safety but entails a trade-off through disinfection by-product (DBP) formation; and (iii) EBM provides important complementary insight into mixture toxicity and supports chemical risk interpretation, especially when toxicological data are incomplete. By expressing all risks in Disability-Adjusted Life Years (DALYs), the framework enables quantitative evaluation of these trade-offs and supports the transition toward holistic, risk-based drinking water safety management consistent with the objectives of the SafeCREW project.



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Abbreviations

AT	Average Time	QCRA	Quantitative Chemical Risk Assessment
BDCM	Bromodichloromethane	QMRA	Quantitative Microbial Risk Assessment
BQ	Benchmark Quotient	QSAR	Quantitative Structure
BW	Body Weight	RBF	Riverbank Filtration
CALUX	Chemically Activated Luciferase Expression (bioassay)	RE	Responsive Element (in CALUX assays)
CDBPs	Chlorinated Disinfection By-Products	SF	Slope Factor (for carcinogenic risk)
CDI	Chronic Daily Intake	SD	Standard Deviation
CS	Case Study	SPE	Solid Phase Extraction
DALY	Disability-Adjusted Life Year	STEC	Shiga-toxin-producing E. coli
DBCM	Dibromochloromethane	TBM	Bromoform (Tribromomethane)
DBP	Disinfection By-Product	TCM	Chloroform (Trichloromethane)
DOC	Dissolved Organic Carbon	TD	Time of Death process (in chemical DALY equation)
DW	Drinking Water	TC	Time of Cure (in chemical DALY equation)
DWTP	Drinking Water Treatment Plant	THB	Total Heterotrophic Bacteria
DWDN	Drinking Water Distribution Network	THM / THMs	Trihalomethane(s)
EBM	Effect-Based Monitoring	TOC	Total Organic Carbon
EBT	Effect-Based Trigger value	UF	Ultrafiltration
ED	Exposure Duration	UV/VIS	Ultraviolet/Visible spectroscopy
EF	Exposure Frequency	V _{sample} / V _{eluate}	Sample and eluate volumes (for concentration correction)
EHEC	Enterohaemorrhagic Escherichia coli	WHO	World Health Organization
GAC	Granular Activated Carbon	WP	Work Package
HAA	Haloacetic Acid	YLD	Years Lived with Disability
HRT	Hydraulic Residence Time	YLL	Years of Life Lost
HUS	Hemolytic Uremic Syndrome		
IR	Ingestion Rate		
LB	Lower Bound		
LOD	Limit of Detection		
LR	Life-related durations		
LRV	Log Removal Value		
MAR	Managed Aquifer Recharge		
MLE	Maximum Likelihood Estimation		
MLELC	Maximum Likelihood Estimation for Left-Censored Data		
MoA	Mode of Action		
N50	Median Infectious Dose (dose-response model parameter)		
NOM	Natural Organic Matter		
PAH	Polycyclic Aromatic Hydrocarbon (bioassay)		
PDF	Probability Density Function		
PFU	Plaque-Forming Units		
PFOA	Perfluorooctanoic Acid		
PXR	Pregnane X Receptor bioassay		



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1. Introduction and aim of the task

The management of drinking water systems increasingly relies on risk-based approaches to ensure the protection of public health under variable and often uncertain conditions. Rather than focusing solely on compliance with concentration limits, risk-based frameworks aim to quantify the actual health burden associated with different hazards and to support proportionate, evidence-based decisions. Chemical disinfection represents a paradigmatic example of the need for such an approach. While the application of disinfectants such as sodium hypochlorite is indispensable for biologically unstable water and acute events to control pathogenic microorganisms and meet stringent microbiological health targets, it simultaneously promotes the formation of disinfection by-products (DBPs), including trihalomethanes, which are associated with long-term chemical health risks. This creates an inherent trade-off: measures implemented to reduce acute microbial risk may increase chronic chemical risk. Managing this balance requires an integrated assessment capable of quantifying both dimensions of risk within a common framework.

Quantitative Microbial Risk Assessment (QMRA) and Quantitative Chemical Risk Assessment (QCRA) provide structured methodologies to estimate, respectively, the health burden from pathogenic microorganisms and from chemical contaminants. However, despite their conceptual compatibility and their shared objective of informing health-based decision-making, these approaches are rarely applied in combination. Methodological differences, divergent exposure assumptions, variability in dose–response modeling, differences in time horizons (acute versus chronic effects), and uncertainties in translating outcomes into comparable health metrics have limited their joint implementation. To understand such differences, the first step is the comprehension of the nature of the two related risks.

First, microbial risk is caused by an acute exposure to a pathogen that can translate into the occurrence of an infection and consequently in the development of a disease (Falkinham et al., 2015). On the other hand, chemical risk is caused by prolonged exposure to contamination, which causes a chronic effect on human health in the long-term horizon (WHO Guidelines for Drinking-Water Quality, 2017). Precisely because of this substantial difference in infectious action, the comparison results in a difficult process. Generally, QMRA is calculated on an annual basis, and, on the opposite, QCRA is something that, by having long-term effects, should be quantified on a lifetime horizon, generally 70 years. Therefore, the first challenge addressed in this project is to identify a method for assessing both risks on the same temporal scale, without compromising the consistency and reliability of the results. Furthermore, not only is the time horizon considered different, but also the unit of measurement used for representing risk results: the Disability-Adjusted-Life-Years (DALY) for the QMRA and the Benchmark Quotient (BQ) for QCRA.

In the current literature, some studies provide methods aimed at calculating the risk through a Quantitative Risk Assessment, but they are nowadays still deeply different (for QMRA: Hamilton et al., 2018, Hamilton et al., 2019, Armstrong & Haas, 2008, Teunis & Schijven, 2018, for QCRA: Sang et al., 2019, Zhang et al., 2018, Pan et al., 2014). Only a few studies are attempting to propose methods that integrate microbial and chemical aspects, but also in this case, the proposed solution presents some limitations.

One of the first studies trying to combine microbial and chemical risks using the DALY approach is Havelaar et al. (2000). This study evaluates the effects of ozonation, as disinfection treatment with bromate as DBPs, in a hypothetical drinking water supply surface water in the Netherlands. In this case,



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the investigated system is the water extracted by a river, and the pathogen of concern is the *Cryptosporidium parvum*. The process of DALYs calculation, both for microbiological and chemical aspects, is reported in its four steps, but the bromate evaluation has been done considering again the lifetime exposure, and, on the contrary, the microbiological risk has been calculated considering the traditional annual base horizon. This study represents a solid starting point for undertaking a more in-depth investigation of this method; however, further research is required.

Another important contribution in the literature is given by Tolofari et al. (2022), who investigate building plumbing systems in different scenarios to assess and compare the risk generated from *Mycobacterium avium* complex (MAC) and as DBPs, only THMs and HAAs. In this study, a final framework able to assess both risks with the DALY approach, is successfully provided. However, the system considered is building in general and its plumbing, and the data from sampling are not specifically taken from the point of exposure at which the receptor can be affected by the risk. So, in this way, the limitation is given by the low attention on this aspects. Lastly, it was revealed that the data used were obtained from sporadic monitoring activities, without providing information on the strategy adopted for sampling and quantifying pathogen and DBP concentrations. Consequently, these data may fail to capture the variability of contamination and may result in outcomes characterized by high uncertainty.

Targeted chemical monitoring for QCRA typically measures concentrations of selected individual chemicals, but it can miss unknown compounds, transformation products, and interactions among many substances that co-occur at low levels. Effect-based monitoring (EBM) represents a complementary methodology to traditional target chemical analyses by using *bioanalytical tools*, such as in vitro cell-based and in vivo whole-organism bioassays, to assess the biological effects of complex mixtures of chemical contaminants present in water samples. These bioassays quantify the *aggregate biological response* elicited by all active chemicals in a sample, capturing mixture effects that would remain undetected by targeted methods alone. To interpret these responses in a risk context, effect-based trigger values (EBTs) are derived by translating existing regulatory benchmarks (e.g., Environmental Quality Standards) into bioanalytical equivalent concentrations that differentiate acceptable from potentially harmful effects. EBM thus provides a hazard-oriented line of evidence that bridges concentration measurements and biological outcomes, offering a more holistic picture of chemical risk that integrates unknowns and mixture interactions.

In this context, it is evident that QMRA, QCRA, and EBM each possess distinct characteristics that complicate direct integration, yet their complementary strengths offer a unique opportunity for a more holistic assessment of health risks in drinking water systems. Table 1 summarizes the key aspects of these methodologies, including their objectives, exposure types, time horizons, measurement units, and inherent advantages and limitations, highlighting how they can collectively inform an integrated, risk-based management framework.



Table 1. Comparison of QMRA, QCRA, and Effect-Based Monitoring (EBM) methodologies, highlighting their objectives, time scales, measurement units, strengths, and limitations in drinking water risk assessment.

Aspect	QMRA (Quantitative Microbial Risk Assessment)	QCRA (Quantitative Chemical Risk Assessment)	EBM (Effect-Based Monitoring)
Objective	Estimate health burden from pathogenic microorganisms (acute infections)	Estimate health burden from chemical contaminants (chronic effects)	Assess aggregate biological effects of complex chemical mixtures in water
Exposure Type	Acute	Chronic / long-term	Variable, reflects cumulative mixture effects
Time Horizon	Typically annual	Lifetime (~70 years)	Flexible; can integrate short- and long-term effects
Measurement Unit	DALY (Disability-Adjusted Life Years)	Benchmark Quotient (BQ) or equivalent chemical risk metric	Bioanalytical equivalent concentration (from effect-based trigger values)
Methodology	Dose–response modeling, exposure assessment	Toxicological reference values, exposure modeling	In vitro cell-based assays, in vivo bioassays, effect-based trigger values
Strengths	Well-established, pathogen-specific, quantitatively interpretable	Regulatory compatibility, chronic risk assessment, long-term hazard quantification	Captures mixture effects and unknown chemicals, biologically relevant, integrates hazard from all active compounds
Limitations	Requires pathogen-specific data, may not capture mixture effects	Only detects monitored chemicals, ignores unknown or interacting compounds	Does not provide specific chemical concentrations, requires calibration with trigger values, interpretation may be context-dependent
Typical Use in Water Management	Assessing disinfection efficacy, outbreak prevention	Evaluating chemical safety, compliance with drinking water standards	Screening for unknown or combined chemical hazards, integrating with chemical monitoring for risk-based decisions

Given this overview and the limited number of studies that systematically attempt to compare microbial and chemical risks within a unified framework, while acknowledging both the innovative advances and the existing methodological gaps, the next step of this project is to develop a detailed and standardized framework for integrated risk assessment in drinking water treatment systems. The proposed framework will encompass treatment processes aimed at ensuring microbiological safety while simultaneously enabling the quantification and management of health risks associated not only with pathogenic microorganisms and treatment-related chemical by-products, but also with the broader biological effects of complex chemical mixtures as revealed through EBM. By jointly addressing microbial, chemical, and effect-based hazard indicators, the framework seeks to support balanced, risk-informed decision-making and to optimize treatment performance within a comprehensive public health protection strategy.



2. Methodological framework and available data for each case study

This section presents the data sources and exploratory analyses conducted in each case study, outlining data availability, sampling frequency, pre-processing steps, and validation of data consistency prior to model development.

2.1. Methodological framework for integrated risk assessment development

2.1.1. Quantitative Microbial Risk Assessment (QMRA)

Regarding the microbial risk, a standardized procedure was adopted to express the risk in terms of DALY. Such procedure is compiled in four steps that are detailed below: i) hazard identification; ii) exposure assessment; iii) dose-response assessment; iv) risk assessment.

Hazard identification

In the hazard identification phase, it is necessary to identify:

- the microbial parameters of interest: in all case studies, *Escherichia coli* was used as an indicator organism for pathogenic *E. coli* in the QMRA. Indicator *E. coli* is widely applied as a proxy for faecal contamination and the potential presence of enteric bacterial pathogens due to its common origin and similar environmental behaviour. In addition, for Berlin case study, *Clostridium perfringens* was selected as an indicator for protozoan transport, while for viral transport somatic phages served as representative. Coliform bacteria are a broad group including *Enterobacter* spp. and *Citrobacter* spp., which naturally occur in soil and decaying vegetation. In a QMRA, using coliforms as a faecal indicator may lead to a false-positive risks, overestimating the presence of enteric pathogens and resulting in unnecessary treatment requirements. Therefore, coliform bacteria were not taken into account in the QMRA.
- the receptors: consumers in building receiving drinking water from the DWDN served by the analysed DWTP.
- the exposure pathway: the selected exposure pathway for the microbial risk assessment was ingestion of contaminated water through faucets.

Exposure assessment

Once the hazard is identified, the exposure assessment phase focuses on determining the dose to which the receptor is exposed, based on both the concentration of the microbial parameter and the frequency of exposure to the risk. To reach such quantification, the description of the analysed case study is the first step (reported in paragraph 2.2).

Dose-response assessment

Estimates of the risk of a response, i.e. infection, illness or death, from a certain dose of a pathogen are calculated by dose-response model. The dose-response models used in this study correspond to the current state of knowledge from QMRAWiki website (<http://qmrawiki.org>).

Risk assessment

The present studies applied the burden of disease and the infection-to-illness risk metrics. The tolerable burden of disease is defined as an acceptable risk of losing no more than one healthy life year in a group of one million people exposed, i.e. a loss of 10^{-6} DALY (disability-adjusted life years) (WHO,



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2011). The threshold for infection probability is defined as the annual probability of infection compared to the benchmark of no more than one person out of 10,000 being infected per year, i.e. 10^{-4} infections per person per year (Schijven et al., 2019). Although both risk benchmarks are commonly used in QMRA to define “safe” water, they measure different outcomes. Infection probability focuses on the occurrence of an event (infection), whereas DALYs focus on the severity of the disease's impact (burden).

2.1.2. Quantitative Chemical Risk Assessment (QCRA) adaptation

Regarding the chemical risk, the objective at this stage of the project was to harmonize the chemical risk quantification process with the one developed for microbiological risk. As a reference model, the study by Pan et al. 2014 was selected. This study proposes a framework for estimating the chemical risk associated with trihalomethanes (THMs) contamination, expressing the results in terms of DALY.

Hazard identification

In the hazard identification phase, it is necessary to identify:

- the DBPs of interest: in both case studies, where QCRA was applied, the DBPs of interest were trihalomethanes (THMs), namely chloroform (CHCl_3), dichlorobromomethane (CHCl_2Br), chlorodibromomethane (CHClBr_2), bromoform (CHBr_3).
- the receptors: consumers in building receiving drinking water from the DWDN served by the analysed DWTP.
- the exposure pathway: DBPs can involve several potential exposure pathways, including inhalation, ingestion, and dermal contact. In this case, the selected exposure pathway for the chemical risk assessment was ingestion of contaminated water through faucets.

Exposure assessment

For the exposure assessment, the description of the analysed case study is the first step (reported in paragraph 2.2).

In the QCRA, the parameter to be calculated is the chronic daily intake (CDI), which relies on the amount of ingested water and the frequency at which exposure occurs, considering the level of contamination present in the system, represented as $\text{mg}/(\text{kg}\cdot\text{d})$.

The applied formula for the calculation is the following:

$$CDI = \frac{C_{DBPs} * IR * EF * ED * f}{BW * AT}$$

Where:

C_{DBPs} , is the concentration of the disinfection by-products measured in the water system, reported in $\mu\text{g}/\text{l}$. Concentration data are collected from monitoring campaign and probabilistic distributions are built. Concentration distributions were fitted including concentration data below the Limit Of Detection (LOD), through the Maximum Likelihood Estimation (MLE) method for left-censored data, as mentioned in Cantoni et al. (2021).



For the other exposure factors, it's necessary to compare them to the conditions used for the microbiological side.

So, here are listed all the parameters and the different assumptions used for the calculations.

- IR is the ingestion rate of drinking water, equal to 2 L/d taken as reference for risk assessment (WHO, 2016). Sensitivity to the IR has been assessed by varying it with national data of drinking water daily consumption for Italy (0.84 L/d) and Ukraine (1.73 L/d) (Penserini et al., 2022).
- f is the unit of measure conversion factor equal to 10^{-3} mg/ μ g
- BW is the body weight equal to 60 kg, taken from the average of European people (Baken et al., 2018).

The following parameters are all factors related to the time of exposure to chemical risk and have been adapted, through several assumptions, to build a standardized framework.

The exposure duration (ED) and exposure frequency (EF) represent the two factors that describe how long people are exposed to the risk. Traditionally, the chemical risk, being a chronic risk, is calculated on a long-term basis, and the directive suggests assuming these two values, respectively, equal to 30 years and 365 days per year, which means that people are exposed every day for 30 years to this kind of hazard.

In this project, the purpose is to align the two risks, so the choice was to adapt the chemical time horizon to the traditional one of microbiological risk, set on an annual basis.

For those reasons, these values will be equal to:

- EF: exposure Frequency of 365 d/y
- ED, for the reasons previously exposed, because we chose to maintain, for both, an annual-based evaluation, it is equal to 1 y.
- AT, that is the average exposure time, always for the same reasons, is considered equal to 365 d.

Dose-exposure assessment

The analysis of the exposure response for the QCRA involves the calculation of the cancer risk (CR). Similarly to the QMRA, the dose–response assessment was performed on an annual basis.

The calculation of CR occurs through the following formula:

$$CR = CDI * SF$$

In this case:

- The endpoint of the health risk assessment is liver cancer following the assumption made for THMs as DBPs (Pan et al., 2018).
- CDI previously calculated
- SF is the slope factor, that is, the parameter used for the calculation of the CR for carcinogenic substances. In this case, for THMs, the Integrated Risk Information System [8] provides SF for each THM:
 - $SF_{TCM} = 6.1 \times 10^{-3} \text{ (mg/kg d)}^{-1}$
 - $SF_{BDCM} = 6.2 \times 10^{-2} \text{ (mg/kg d)}^{-1}$



- $SF_{DBCM} = 8.4 \times 10^{-2} \text{ (mg/kg d)}^{-1}$
- $SF_{TBM} = 7.9 \times 10^{-2} \text{ (mg/kg d)}^{-1}$

Risk assessment

The risk assessment is performed in terms of DALY, using the following equation:

$$DALYs = YLLs + YLDs$$

Where:

YLLs is the value of life-lost years due to premature mortality, given in terms of per person-year (ppy)

$$YLLs = \sum_x n_x * p_x * (1 - S_x) * (e_x^* - T_D)$$

YLDs refer to the years lived with disability given in per person-year (ppy).

$$YLDs = \sum_x n_x * p_x * [(1 - S_x)DW_y * L_y + S_x * (DW_y * L_y + P_{seq} * DW_{seq} * (e_x^* - T_C))]$$

The two time-related factors, T_D and T_C , represent, respectively, the duration of the death process and the duration time for curing the disease, and they are given by the following formula:

$$T_D = L_D + L_{R2} + L_M + L_T$$

$$T_C = L_D + L_{R1}$$

Here are reported the meanings of all the parameters and the applied assumptions.

These two time parameters are the results of summing up the different durations of the disease phases. For T_D , the disease is considered in its entirety, while for T_C , the result is given by the sum of the phases in which the patient is curing the disease.

The different terms in these two calculations, taken from Pan et al., 2018, in years (y) are:

- $L_D = 0.333$ y duration of the diagnosis and preliminary treatment
- $L_{R1} = 3.67$ y duration of the treatment control phase
- $L_{R2} = 1.53$ y duration of the treatment control phase
- $L_M = 0.25$ y duration of the early stage of death
- $L_T = 0.083$ y last stage of death.

To the different durations of the disease phases correspond the different weights of disability, as follows:

- $DW_D = 0.27$
- $DW_R = 0.18$
- $DW_M = 0.64$
- $DW_T = 0.93$

For the calculation of the other components, YLLs and YLDs, several assumptions must be made.

First, these two factors result from a summary of different contributions that are dependent on age groups (x) and disease phase (y).



For both:

- n represents the population in a certain age group. For these values, the information was taken from the cited study in the RIVM report on DALY comparison (2024): Statistics for Italy and Ukraine. The applied value is in terms of the percentage of the age-group population with respect to the total population considered. In this case, only two age classes have been considered, so in the nominator, there is the number of people of the specific age group, and the denominator of the fraction is the result of the sum of the two populations.
- e^* is the standard life expectancy in years. Also, in this case, the same reference was used: Statistics for Italy and Ukraine.
- P refers to morbidity. According to Pan et al. (2018), this parameter is considered the CR previously calculated. Therefore, the calculations were performed with SF reported in Table 1.
- S refers to the survival rate, already given by Pan et al. (2018), equal to 0.8
- $P_{seq} = 0.16$ refers to the proportion of sequelae patients
- $DW_{seq} = 0.188$ is the weight of sequelae disability.

At that point, the chemical risk calculation is completed, and the results in DALYs are achieved.

In Table 1 the new framework developed at this point for QCRA with final DALY calculation is reported.

Table 1. Summary table containing all assumed parameters, with their reference, for the calculation of the QCRA.

Parameter	Value	Unit of measure	Reference
IR	2	L/d	WHO (2016)
EF	365	d/y	assumption
ED	1	y	assumption
f	10^{-3}	mg/ μ g	conversion
BW	60	kg	Baken et al. (2016)
AT	365	d	assumption



2.1.3. Effect-Based Monitoring (EBM)

Effect-Based Monitoring (EBM) was performed in Milan CS, by analysing the same samples analysed for microbial parameters and DBPs. All samples were extracted using the HLB-SPE method for general extraction purposes. The extract is then measured on a panel of CALUX assays. The following CALUX assays were measured: Cytotox, P53, Nrf2, PXR, Era, anti-AR, PAH and TTR-TRb.

The CALUX bioassays comprise human bone cell lines (U2-OS) or rat hepatoma cells (H4IIE), incorporating the firefly luciferase gene coupled to Responsive Elements (REs) as a reporter gene for the presence of compounds able to activate the respective responsive elements. Cells that are exposed to compounds of interest not only express proteins that are under normal circumstances associated to RE, but also luciferase. By addition of the appropriate substrate for luciferase, light is emitted. The amount of light produced is proportional to the amount of ligand-specific receptor binding, which is benchmarked against the relevant reference compounds (see Table 2).

Table 2. Human cell line-based CALUX bioassays used to analyse total bioactivity of DWTP samples.

Bioassays	Pathway activation	Reference compound	CAS no.
Cytotox	Cytotoxicity (modulation of constitutive transcription)	TBT	56-36-0
P53	Genotoxicity (P53-dependent pathway activation)	Actinomycin D	50-76-0
Nrf2	Oxidative stress induction (Nrf2 pathway activation)	Curcumin	458-37-7
PXR	Xenobiotic metabolism (PXR activation)	Nicardipin	54527-84-3
ER	Hormone mediated MoA (estrogen activity)	17 β -Estradiol	50-28-2
anti-AR	Hormone mediated MoA (anti-androgen activity)	Flutamide	13311-84-7
PAH	Dioxin receptor activation	Benzo-a-Pyrene	50-32-8
TTR-TRb (ref = PFOA)	Competitive binding of Thyroid hormone transporter	PFOA	335-67-1



2.2. Data sources and assumptions for each case study

2.2.1. Data for QMRA application in CS#1 – Berlin, Germany

Case study site description

The case study CS1B is situated in the north-western part of Berlin (Germany) at the waterworks Berlin-Spandau. Site description is found in Sprenger and Wullenweber (2024) (SafeCrew D2.1) and Sprenger (2021). A hydrogeological cross-sectional view based on water level measurements from 2014-2016 (Sprenger, 2018) and geological explorations (Brühl and Limberg, 1985) is depicted in Figure 1.

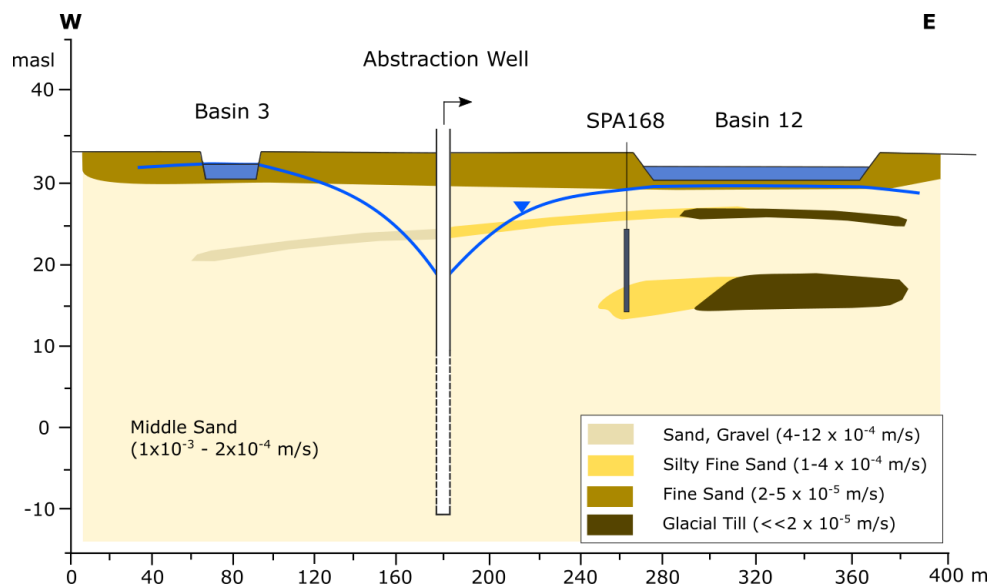


Figure 1. Hydrogeological cross-section at the sampled abstraction well and recharge basins at waterworks Spandau (vertical exaggeration 1:5) (modified from Sprenger (2021))

Microbial field sampling was conducted over a 13-month period, from August 2023 to August 2024. While the monitoring plan called for continuous monthly monitoring over one annual cycle, the January 2024 campaign was cancelled due to illness among the personnel. Water samples were collected from the recharge basin (Basin 12), the observation well (SPA168), and a production well to analyse microbial indicators, specifically *Coliform bacteria*, *Escherichia coli*, *Enterococci*, somatic coliphages, and *Clostridium perfringens*. All microbial analyses were carried out by Berliner Wasserbetriebe's (BWB) accredited microbiology laboratory.

Samples from the recharge basin were taken by conventional methods, while the groundwater sampling points (observation well and well) were analysed using hollow-fiber ultrafiltration systems (REXEED-25A dialysis filter). Approximately between 100 and 300 litres of groundwater were collected in the observation well and well using ultrafiltration-based microbial enrichment. At the BWB laboratory, the ultrafiltration modules were eluted to reduce the total sampled volume to 400 ml. This was then separated into 100 ml portions, from which the microbial parameters were measured.



The ultrafiltration module was operated at a maximum flow rate of 2 L/min. Up to 314 litres of groundwater were filtered without any significant change in the flow rate. Samples were transported to the laboratory by 2pm on the same day of sampling. Microbial analysis was conducted within 24 hours upon arrival. Further information about the enrichment method is described in Korth et al. (2017). Measured concentrations are corrected for recovery and sampled volume to estimate original groundwater concentrations according to:

$$C = \frac{C_{\text{Eluate}} \times V_{\text{Eluate}}}{V_{\text{Sample}} \times R}$$

Where:

C = final concentration (e.g. CFU /100 ml)

C_{Eluate} = measured concentration in the final extract (e.g. CFU /100 ml)

V_{Eluate} = final extract volume (mL)

V_{sample} = groundwater sample volume (mL)

R = recovery rate (dimensionless)

Figure 2 illustrates the distribution of coliform bacteria, *Escherichia coli*, enterococci, somatic coliphages, and *Clostridium perfringens* measured at the recharge basin, observation well, and abstraction well. Only concentrations above the limit of quantification are shown. The numbers displayed at each sampling location indicate the total number of measurements and the corresponding number of samples with positive detections. At the recharge basin, 12 samples were collected for all microbial parameters. The observation well was sampled over 11 months, as sampling was temporarily limited by elevated turbidity. Sampling at the abstraction well was discontinued after 5 months to allow for extended enrichment efforts at the observation well.



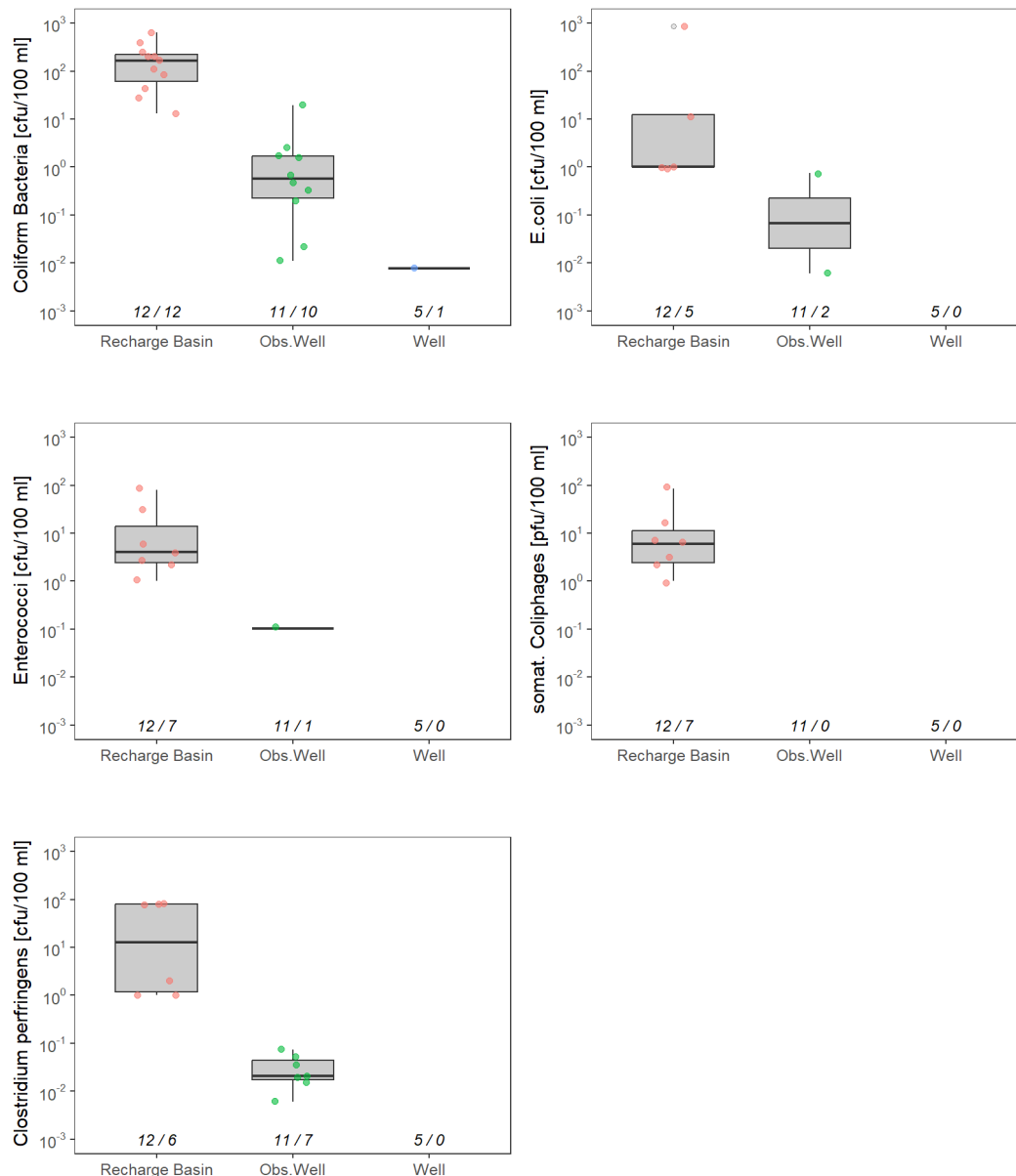


Figure 2: Distribution of Coliform bacteria, *Escherichia coli*, Enterococci, somatic coliphages, and *Clostridium perfringens* measured at the Recharge Basin, Observation Well (Obs. Well), and Well. The numbers at each sampling location denote the total number of measurements / number of samples with positive detection. The data points (dots) show the individual sample concentrations.

The highest concentrations and detection frequencies occur at the recharge basin. *E. coli* and enterococci, which are used as indicators of faecal contamination, show marked reductions in the observation well and are absent in the abstraction well. These results suggest that vegetative bacteria are effectively attenuated during their passage through the subsurface, which is consistent with their relatively low environmental persistence. The maximum concentrations of *E. coli* and enterococci in the recharge basin were 866 cfu/100 ml and 80 cfu/100 ml, respectively.



Clostridium perfringens, which serve as indicators for protozoan transport, exhibit lower concentrations in the recharge basin but remain detectable at the observation well. The presence in the observation well indicates greater resistance to environmental stress compared to bacterial indicators. However, the absence at the abstraction well suggests that the aquifer still provides substantial reduction capacity for more persistent microorganisms. The maximum concentration of *Clostridium perfringens* in the recharge basin is 80 cfu/100 ml.

Coliform bacteria are a broad group including *Enterobacter* and *Citrobacter*, which naturally occur in soil and decaying vegetation. In a QMRA, using coliforms as a faecal indicator may lead to a false-positive risks, overestimating the presence of enteric pathogens and resulting in unnecessary treatment requirements. Therefore, coliform bacteria were not taken into account in the QMRA.

While somatic coliphages reached a maximum concentration of 86 pfu/100 mL in the recharge basin, no positive detections were observed in the observation or production wells, even with the enhanced sensitivity provided by sample enrichment

Ultrafiltration-based enrichment substantially improves the estimation of log removal rates (LRV) compared to conventional sampling approaches. For a sample volume of 100–314 L, the corrected concentration lies between 0.008 and 0.003 counts per 100 mL, respectively.

E. coli as indicator for bacterial transport and *Clostridium perfringens* as an indicator for protozoan transport is used for the estimation of site-specific LRV. Somatic coliphages were utilized as viral surrogates to determine a minimum Log Reduction Value (LRV). Since no phages were detected in the groundwater, the calculated LRV represents the lower bound of the system's removal capacity based on the analytical limit of detection.

Log Reduction Values (LRV) subsurface

The QMRA is conducted with various Log Reduction Values (LRV) for the subsurface passage related to the Hydraulic Residence Times (HRT) and for each pathogen group separately. HRT was determined previously by temperature and stable isotope measurements (Sprenger, 2018). HRT was found to be 54-61 days (± 11 d) in the well and about 8 days in the observation well.

To appropriately account for measurements below the detection limit, concentration data were modelled using a negative binomial distribution within a Bayesian framework. Model estimation was performed in R using the package *brms*, which fits Bayesian multilevel models via the probabilistic programming language Stan (Bürkner, 2017). The use of the “negbinomial2” model allowed explicit simulating overdispersed count data while retaining information from low concentration measurements. This approach avoids ad-hoc substitution methods (e.g., replacing non-detects with zero or half the detection limit) and instead incorporates uncertainty associated with low-concentration samples directly into the likelihood. As a result, parameter estimates and derived quantities, such as log removal values, are statistically robust and not biased toward artificially inflated or deflated values in the presence of near-detection-limit observations. In a Bayesian framework, model parameters are not estimated as single point values but as posterior distributions that reflect uncertainty given the observed data. The posterior predictive distribution represents the distribution of replicated observations that could be generated from the fitted model. In practice, posterior predictive samples are obtained by drawing repeatedly from the posterior distribution of model parameters and, for each draw, generating a predicted concentration value. This results in a distribution of plausible concentrations that reflects both natural variability and parameter uncertainty.



Separate Bayesian negative binomial models were fitted to the data from the recharge basin and the observation well. Each model yields a posterior predictive distribution, which represents the range of concentrations that are consistent with the observed data at each location. The posterior predictive distribution for the recharge basin characterises plausible influent concentrations entering the subsurface system. The observation well posterior predictive distribution characterises the likely concentrations after 8 days of subsurface attenuation (HRT = 8). A graphical display of the simulated *E. coli* concentrations is shown in Figure 3.

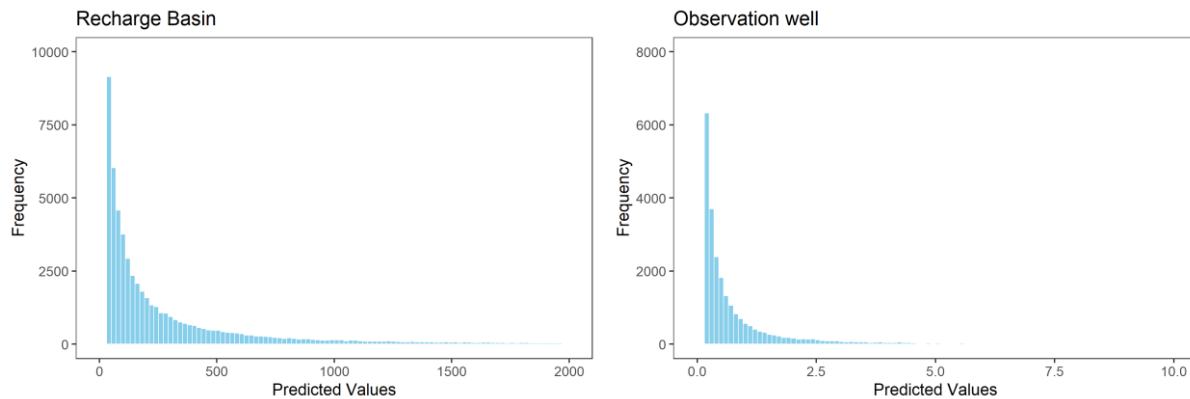


Figure 3: Posterior distribution from negative binomial model for *E. coli* in the recharge basin and observation well.

Rather than computing LRV from single summary statistics (e.g. sample means), the Bayesian approach computes LRVs draw-by-draw using posterior predictive quantities. The resulting LRV distribution reflects uncertainty in both recharge basin and observation well concentrations. Distribution of the log removal value (LRV) for *E. coli* is shown in Figure 4.

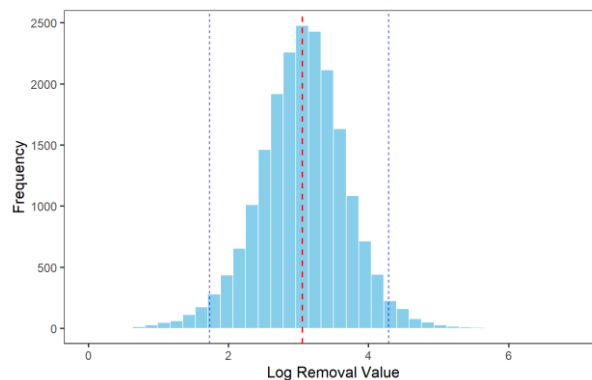


Figure 4: Distribution of the log removal value (LRV), defined as $\log_{10}(\text{surface water concentration} / \text{groundwater concentration})$, based on *E. coli* posterior prediction from Bayesian negative binomial models. Red line = median; blue dotted lines = upper and lower 95 percentile.



After an HRT of eight days, the median LRV for *E. coli* was found to be 3.07 (sd = ± 0.64) as measured in the observation well. This finding is used to inform the subsurface removal of bacteria. Accordingly, the LRV for *Clostridium perfringens* was calculated, as shown in Figure 5 and Figure 6.

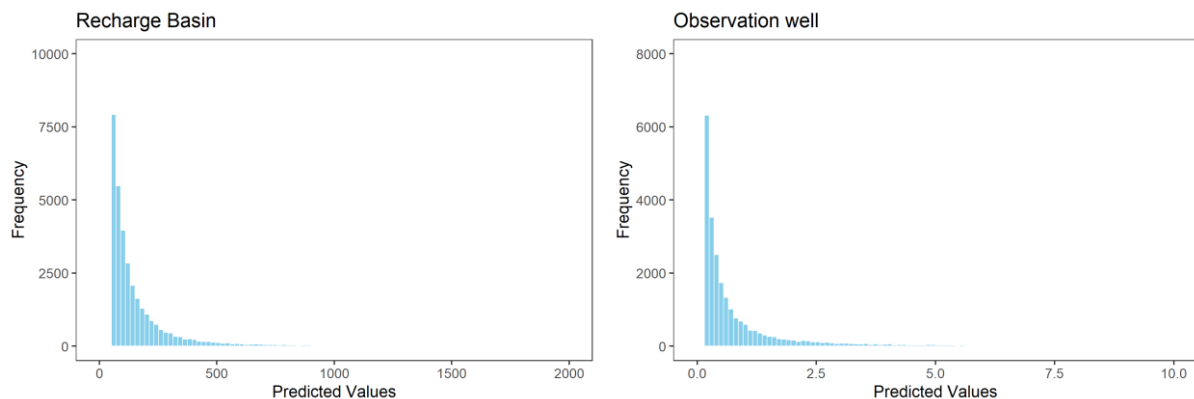


Figure 5: Posterior distribution from negative binomial model for *clostridium perfringens* in the recharge basin and observation well.

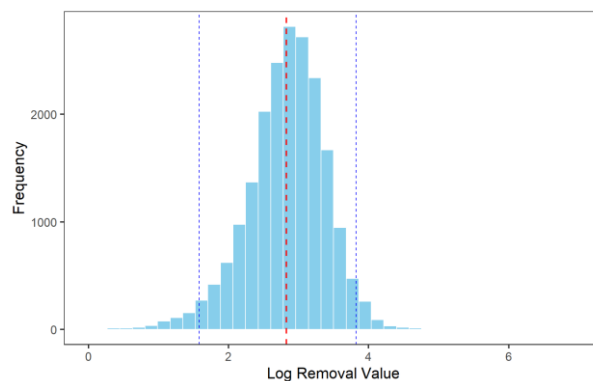


Figure 6: Distribution of the log removal value (LRV), defined as $\log_{10}(\text{surface water concentration} / \text{groundwater concentration})$, based on *clostridium perfringens* posterior prediction from Bayesian negative binomial models.

After an HRT of eight days, the median LRV for *clostridium perfringens* was found to be 3.33 (sd = ± 0.40) as measured in the observation well. This finding is used to inform the subsurface removal of protozoa.

Viral transport could not be assessed by measurements due to a lack of positive detection in the observation well. Instead, the minimum LRV was calculated based on non-detection in the observation well using the detection limits and a conservative source concentration from the recharge basin. The measured median concentration of somatic phages was found to be 6 pfu/100 ml. Based on the improved detection limit of between 0.008 and 0.003 organisms/100 ml, the minimum LRV ranges from 2.87 to 3.30. The lowest LRV is used to inform the subsurface removal of viruses.



Typically, the reduction of microorganisms during subsurface transport is characterised by biphasic kinetics. As shown in the literature, e.g. Pang (2009) and Wielen et al. (2008), microbial removal generally exhibits a biphasic pattern: an initial phase of rapid removal is succeeded by a secondary phase characterised by a substantially reduced removal rate. To account for LRV upscaling to higher HRT in subsurface the maximum achievable log removal is calculated according to:

$$LR(t) = LR_{\max}(1 - e^{-\alpha t})$$

Where:

$LR_{\max}$ = maximum achievable log removal

α = decrease constant

The uncertainty of log removal was quantified using the coefficient of variation derived from the measured log removal at 8 days HRT. This coefficient was assumed constant over hydraulic residence time, resulting in a proportional uncertainty propagation according to:

$$c_v = \frac{sd_{t=8}}{LR_{t=8}}$$

$$sd(t) = c_v \times LR_{\text{med}}(t)$$

Where:

c_v = coefficient of variation

sd = standard deviation

The log removal rate as a function of the hydraulic residence time is shown as an example for *E. coli* (Figure 7).

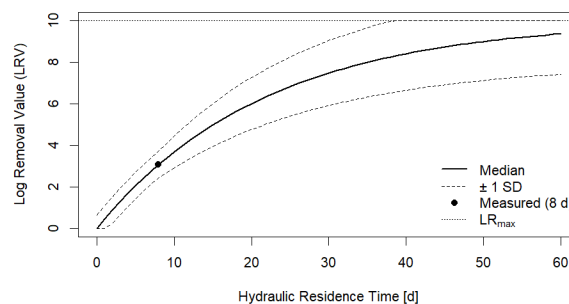


Figure 7: Log removal as a function of hydraulic residence time. Cap-limit log-removal model with an asymptotic maximum log removal ($LR_{\max}$); solid line shows the median, dashed lines ± 1 standard deviation, dotted line $LR_{\max}$, and the dot the measured value at 8 days.

A first-order degradation model assumes unlimited removal and therefore predicts a linear, unlimited increase in log removal with residence time, which can lead to unrealistically high values at longer travel times. In contrast, the cap-limit log-removal model explicitly accounts for physical, chemical, and biological constraints in groundwater systems by imposing a maximum achievable log removal. As a result, the cap-limit model provides more realistic and conservative predictions at longer residence times while still reproducing first-order-like behaviour at shorter residence times.



To prevent high log-removal values at longer hydraulic residence times, a limit of 10 log₁₀ removal was applied to all pathogen groups. The median log-removal values (LRVs) approach the cap asymptotically with increasing residence time, while uncertainty increases at longer hydraulic residence times (HRTs). LRVs at an HRT of 8 days are based on measurements, while those at other HRTs are modelled (Table 1).

Table 1: Calculated log-removal values (LRV) as a function of hydraulic residence time (HRT) for viruses, bacteria, and protozoa using a cap-limit log-removal model with an upper removal limit of 10 log₁₀.

HRT [days]	Virus		Bacteria		Protozoa	
	LRV _{med}	±1 sd	LRV _{med}	±1 sd	LRV _{med}	±1 sd
8	2.87	0.45	3.07	0.64	3.33	0.40
20	5.52	0.86	5.81	1.21	6.17	0.74
30	7.06	1.10	7.35	1.53	7.69	0.92
40	8.07	1.26	8.32	1.73	8.61	1.03
50	8.74	1.37	8.94	1.86	9.16	1.10

Inflow concentrations

Total variability in pathogen concentration for inflow concentration is difficult to assess, because it can be unclear whether measurements cover the full range of microbial concentration. Low pathogen concentrations and the irregular occurrence of pathogens contributes to the difficulties in capturing this variability.

Somatic coliphages were used as viral indicators to estimate the concentrations of pathogenic viruses in the inflow (i.e. recharge basin). Pathogen concentrations were derived by applying virus-to-phage ratios from literature. Pathogenic human viruses have been reported to occur at concentrations approximately 500-fold lower than somatic coliphages in water environments, although substantial variability has been observed (WHO, 2022). Based on this relationship, the concentrations of pathogenic viruses were conservatively estimated to be 0.2% of the concentrations of somatic coliphages that were measured (WHO, 2022). Rotavirus was selected as the reference pathogenic virus for the QMRA because it is a well-established cause of acute gastroenteritis and being excreted in high concentrations by infected individuals. It has been widely used in QMRAs as a representative enteric virus due to the availability of dose–response models, enabling quantitative estimation of infection risk. The maximum inflow concentration was derived by applying virus-to-phage 1/500 ratio to the maximum observed somatic coliphage concentration (860 pfu/L), yielding an estimated maximum concentration of 1.72 organism/L.

Direct correlations of the measured concentration of *Clostridium perfringens* with enteric pathogens like *Cryptosporidium parvum* are found to be inconsistent in the literature. In the absence of direct protozoan monitoring data for the River Havel (Berlin), source water concentrations of *Cryptosporidium parvum* oocysts were estimated using surface water and river monitoring studies from other German rivers. Data from the Lower Rhine indicate *Cryptosporidium* oocyst detections ranging from 0 to 25 per 100 L (Gallas et al., 2012). These ranges (0-0.25 organism/L) were used to define probabilistic source terms in the QMRA model. This approach is expected to overestimate protozoan concentrations and therefore represents a deliberately conservative assumption for the QMRA.



Escherichia coli was used as an indicator organism for pathogenic *E. coli* in the QMRA. Indicator *E. coli* is widely applied as a proxy for faecal contamination and the potential presence of enteric bacterial pathogens due to its common origin and similar environmental behaviour. In this study, concentrations of pathogenic *E. coli* were estimated that a conservative fraction (e.g. 3%) of the total *E. coli* concentration is pathogenic (Haas et al., 1999). This approach provides a realistic yet protective estimate of bacterial health risk, aligning with empirical observations where only a small subset of the *E. coli* population causes human disease.

The estimated inflow concentrations are transferred to uniform distribution. With the uniform distribution, all values within the given ranges will have the same probability of occurrence. Ensuring a conservative approach.

Exposure assessment

End-use of the abstracted water is drinking water. The volume of ingested water is assumed to be 1-3 L/d. A triangular distribution with modal value of 2 L/d and 365 days per year consumption was assumed. It is assumed that the recovered water is consumed without any technical post-treatment.

Burden of disease and ratio of infection to illness

While most *E. coli* strains do not cause human disease, some strains may cause life-threatening conditions. Enterohemorrhagic *E. coli* (EHEC) has been implicated in a number of cases of hemolytic colitis (diarrhea) and hemolytic uremic syndrome (HUS) in industrialised countries. EHEC are bacteria that are capable of producing cytotoxins, the shiga-like toxins. They are summarised under the term shigatoxin-producing *E. coli* (STEC). The most significant STEC serogroup worldwide and in Germany is the O157 strain (RKI, 2021). It must be noted that only a small fraction of *E. coli* are pathogenic. However, in this QMRA it is assumed that all *E. coli* are pathogenic. The burden of disease per symptomatic cases for shiga-toxin producing *E. coli* O157 was based on data from the Netherlands from 1999-2000 as calculated in Havelaar and Melse (2003).

The QMRA modelling applied a stochastic Monte Carlo simulation process performed within the R programming language (R-CoreTeam, 2021) by using the R package “kwb.qmra (v0.3.0)” (Rustler et al., 2021). All input parameters included in the QMRA model were presented as probability distribution functions (PDFs) and sources (Table 2).



Table 2: Input parameters for quantitative microbial risk assessment (QMRA) for the CS#1 Berlin

Parameter		Value	PDF	Reference / Source
Inflow concentration (organism/L) in recharge basin	<i>E. coli</i> (bacteria)	Min = 0; Max = 260	uniform	site-specific 3% pathogenic (Haas et al., 1999) of maximum measurements
	Somatic Coliphages (virus)	Min = 0; Max = 1.72 pfu/L	uniform	site-specific based on maximum measurements, indicator-to-pathogen ratio 1/500 (WHO, 2022)
	<i>Clostridium perfringens</i> (protozoa)	Min = 0; Max = 0.25	uniform	Measurements in lower Rhine river (Gallas et al., 2012)
Log Reduction Value (LRV) aquifer passage	Bacteria	3.07±0.64 (HRT = 8d)	Normal	site-specific based on <i>E. coli</i>
	Virus	>2.87±0.45 (HRT = 8d)	Normal	site-specific based on somatic phages
	Protozoa	3.33±0.40 (HRT = 8d)	Normal	site-specific based on <i>Clostridium perfringens</i>
Ingestion in L/d		Drinking water: Min=1; Max = 3; Mode = 2	Triangle	(WHO, 2006)
Number of events in d/yr		Every day consumption: 365	Constant value	-
Dose–response	<i>E. coli</i>	$\alpha = 1.55\text{E-}01$, $N_{50} = 2.11\text{E}+06$	Beta-Poisson	DuPont et al. (1971) from QMRAwiki
	<i>Rotavirus</i>	$\alpha = 0.253$, $N_{50} = 6.17$	Beta-Poisson	Ward et al. (1986) from QMRAwiki
	<i>Cryptosporidium parvum</i>	$k = 0.0572$	Exponential	Messner et al. (2001) from QMRAwiki
Ratio of illness/infection	<i>E. coli</i>	0.25 (based on Shigella)	Constant value	Table 6 in Howard et al. (2006)
	<i>Rotavirus</i>	0.5	Constant value	Table 8 in Howard et al. (2006)
	<i>Cryptosporidium parvum</i>	0.3	Constant value	Table 8 in Howard et al. (2006)
Disease burden per case (DALYs per person per case)	<i>E. coli</i>	0.0547 (Shiga-toxin producing <i>E. coli</i> O157)	Constant value	Table 2.7 in Havelaar and Melse (2003)
	<i>Rotavirus</i>	0.014	Constant value	Table 2.12 in Havelaar and Melse (2003)
	<i>Cryptosporidium parvum</i>	0.0013	Constant value	Table 2.2 in Havelaar and Melse (2003)

PDF = probability density function; LRV = Log Reduction Value; DALY = Disability-Adjusted Life Years



2.2.2. Data for QCRA and QMRA application in CS#4 – Western Ukraine, Ukraine

Restrictions due to martial law

Due to the ongoing state of martial law in Ukraine, it should be noted that access to and disclosure of certain technical, infrastructural and geospatial information is legally restricted. In accordance with national security regulations, detailed data relating to the exact location of water supply infrastructure such as well coordinates is classified. Consequently, the present study only reports aggregated, generalised or anonymised information that is sufficient for scientific interpretation, while avoiding the disclosure of sensitive details. These limitations do not affect the validity of the conceptual hydrogeological framework or the interpretation of the discussed riverbank filtration processes.

Case study site description

The water supply system is based on riverbank filtration (RBF) wells located at the confluence of two rivers within an extensive floodplain. The rivers originate in the Eastern Beskids, a mountainous region characterised by relatively high levels of precipitation and seasonal flow variability. The confluence setting enhances the hydraulic connectivity between surface water and the adjacent alluvial aquifer, making the site favourable for induced bank infiltration (Figure 8).

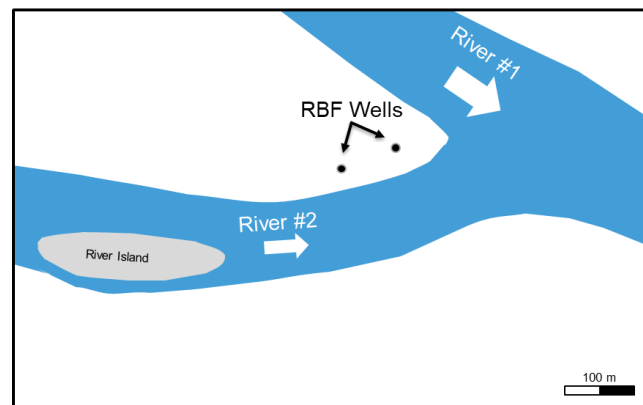


Figure 8: Conceptual schematic of the riverbank filtration (RBF) setting at the confluence of two rivers. River #1 and River #2 converge within a floodplain environment, with flow directions indicated by arrows.

The hydrogeological setting consists predominantly of Quaternary alluvial deposits made up of unconsolidated sand and gravel. These sediments have high hydraulic conductivity and porosity, which enables river water to infiltrate the aquifer efficiently. The unconfined alluvial aquifer is hydraulically connected to the river system, and the flow of groundwater is strongly influenced by fluctuations in the river stage and abstraction from the RBF wells.

The RBF wells are constructed to a depth of approximately 20 m below ground surface and are screened within the permeable sand and gravel layers. Abstraction from the wells induces infiltration of river water through the riverbed and bank sediments, resulting in a mixture of bank-filtered surface water and ambient groundwater. The average abstraction rate is approximately 720 m³/day per well, which is sufficient to maintain a stable contribution of infiltrated river water.

During subsurface passage, the infiltrating river water undergoes a range of physical, chemical, and biological attenuation processes, including particulate filtration, sorption, and microbial degradation. These processes contribute to the improvement of raw water quality, particularly with respect to turbidity, suspended solids, and selected organic and microbiological contaminants.



Following abstraction, the bank-filtered water is subjected to post-treatment consisting of disinfection using sodium hypochlorite. Dissolved iron levels remained below 0.5 mg/L, reflecting the sub-oxic conditions of the groundwater. No additional physical or chemical treatment steps are applied. Disinfection is implemented to ensure microbiological safety and compliance with drinking water quality standards, particularly during periods of elevated river discharge or flooding when pathogen loads in surface water may increase.

Hydraulic residence time of bank filtered water

Heat transport in the riverbank filtration system is governed primarily by advective groundwater flow and conductive heat transfer through the solid matrix of the aquifer. Advective heat transport occurs as infiltrating river water moves through the pore spaces of the alluvial sand and gravel, transferring thermal signals downstream along groundwater flow paths. In contrast, heat conduction through solid materials and the pore water acts to dampen temperature fluctuations and smooth temporal variations. The relative contribution of advection and conduction depends on groundwater velocity, sediment thermal properties, and the degree of hydraulic connectivity between the river and the aquifer. In highly permeable alluvial deposits, advective transport typically dominates, allowing seasonal surface water temperature signals to propagate into the aquifer with a measurable time lag. By monitoring the thermal signal on-site, the resulting attenuation and phase shift allowed for the estimation of HRT using temperature as a natural tracer (Figure 9).

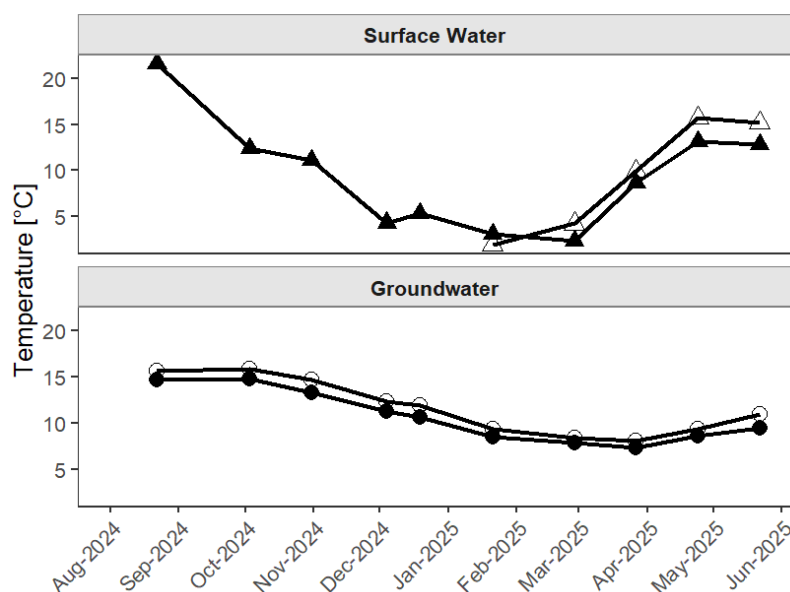


Figure 9: Seasonal variation in surface water and groundwater temperature at the riverbank filtration site used to assess hydraulic residence time (HRT) by heat tracing. The black and white symbols represent the two rivers and abstraction wells, respectively.

Analysis of the temperature time series indicates a clear temporal lag between the minimum surface water temperature in winter and the corresponding minimum in groundwater. This lag time was found to be around 65 days. To account for the thermal retardation caused by heat exchange between the pore water and the solid aquifer matrix, a thermal retardation factor of two was assumed, which is consistent with the values reported for unconsolidated sand and gravel aquifers (Anderson, 2005). Applying this correction yields an effective hydraulic residence time (HRT) of around 32.5 days for the riverbank filtration system.



Monitoring campaign for microbial and chemical water characterization

From August 2024 to May 2025, monthly sampling of microbial parameters (total coliforms, *E. coli*, enterococci, coliphages, salmonella, *Pseudomonas aeruginosa* and total microbial count at 37 °C) and chemical ones (Chloroform (TCM), Bromodichloromethane (BDCM), Dibromochloromethane (DBCM); Bromoform (TBM)) was conducted by NUWEE in surface water, in two wells after riverbank filtration, after disinfection with sodium hypochlorite, and in five location in the Drinking Water Distribution Network (DWDN). As for microbial characterization, positive findings were detected only for total coliforms and *E. coli* in surface water samples, while other microbiological parameters were below the detection limit. Thus, *E. coli* is used for the following QMRA based on the measurement (Figure 10).

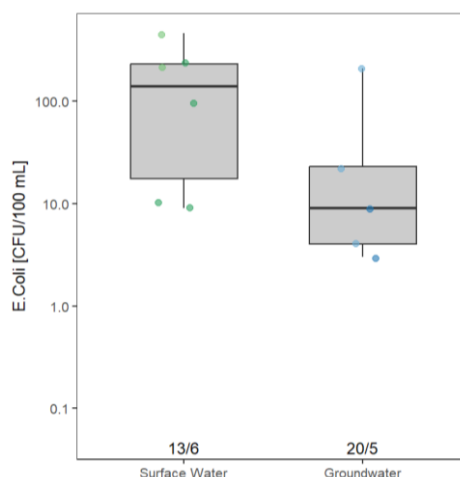


Figure 10: *Escherichia coli* concentrations [CFU/100 mL, log-scale] measured in surface water and groundwater (RBF wells before disinfection). Boxplots represent the median, interquartile range, and minimum–maximum values, while individual points indicate single sampling events. The numbers at each category denote the total number of measurements / number of samples with positive *E. coli* detection.

Log Reduction Values (LRV) subsurface

By using *E. coli* as the only indicator, it is crucial to explicitly acknowledge the associated uncertainties, and avoid overinterpreting of the results as definitive measures of safety or compliance with regulatory targets. Therefore, a Bayesian approach to quantify uncertainties is applied. In Bayesian modelling, uncertainty is propagated by using posterior samples instead of point estimates. Separate Bayesian negative binomial models were fitted to the data from the surface water and the abstraction well. Each model yields a posterior predictive distribution, which represents the range of concentrations that are consistent with the observed data at each location (Figure 11).

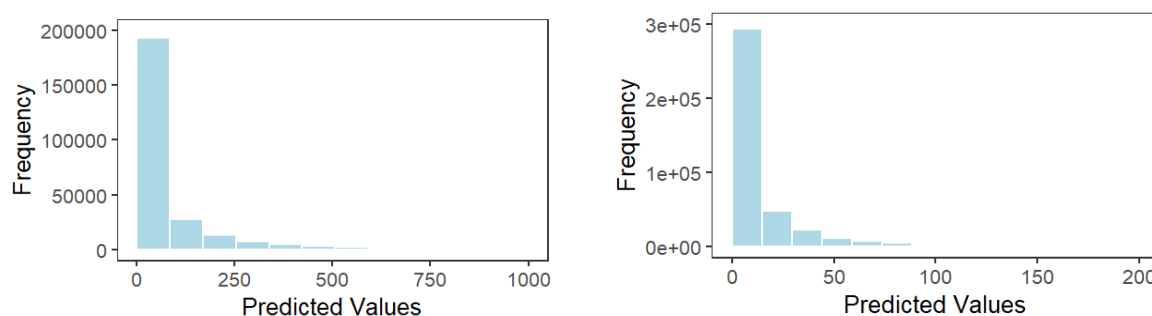


Figure 11: Posterior distribution from negative binomial model for *E. coli* in the surface water (left) and abstraction wells (right).



Rather than computing the LRV from a single summary statistic (e.g. the sample mean), the Bayesian approach computes the LRV using posterior predictive quantities. The resulting LRV distribution reflects uncertainty in surface water and abstraction well concentrations. The mean LRV for *E. coli* was found to be 0.78, with upper and lower 95% percentiles of 1.39 and 0.22, respectively (Figure 12). This finding informs subsurface bacterial removal.

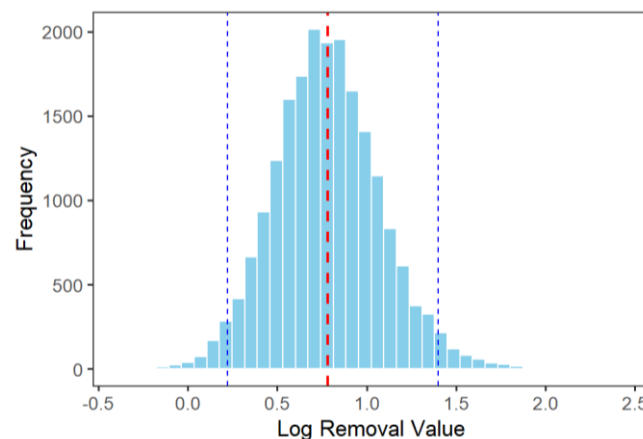


Figure 12: Posterior distribution of the log removal value (LRV), defined as $\log_{10}(\text{surface water concentration} / \text{groundwater concentration})$, derived from Bayesian negative binomial models. The histogram shows the frequency of posterior draws. The red dashed line indicates the posterior median LRV, and the blue dashed lines represent the upper and lower 95% percentile, reflecting uncertainty propagated from both surface water and groundwater models.

Case Study Specific QMRA input parameters

Pathogenic *E. coli* concentrations were estimated by applying a 3% pathogenic fraction (Haas et al., 1999) to the maximum measured total *E. coli* concentration of 460 cfu/100 mL. Monte Carlo-based QMRA was implemented using the R package 'kwb.qmra' (Rustler et al., 2021); input parameters and their respective PDFs are summarized in Table 3.

Table 3: Input parameters for quantitative microbial risk assessment (QMRA) of Riverbank Filtration site in Ukraine

Parameter		Value	PDF	Reference / Source
Inflow concentration (organism/L) in recharge basin	<i>E. coli</i> (bacteria)	Min = 0; Max = 138	uniform	site-specific 3% pathogenic (Haas et al., 1999) of maximum measurements
Log Reduction Value (LRV) aquifer passage	Bacteria	0.76 (sd = 0.29)	Normal	site-specific based on <i>E. coli</i>
Ingestion in L/d		Drinking water: Min=1; Max = 3; Mode = 2	Triangle	(WHO, 2006)
Number of events in d/yr		Every day consumption: 365	Constant value	-
Dose-response	<i>E. coli</i>	$\alpha = 1.55\text{E-}01$, $N_{50} = 2.11\text{E+}06$	Beta-Poisson	DuPont et al. (1971) from QMRWiki
Ratio of illness/infection	<i>E. coli</i>	0.25 (based on Shigella)	Constant value	Table 6 in Howard et al. (2006)
Disease burden per case (DALYs per person per case)	<i>E. coli</i>	0.0547 (Shiga-toxin producing <i>E. coli</i> O157)	Constant value	Table 2.7 in Havelaar and Melse (2003)



2.2.3. Data for QMRA, QCRA and EBM application in CS#2 – Milan, Italy

Case study site description

In Milan CS, drinking water is abstracted from groundwater sources and treated in 28 drinking water treatment plants (DWTPs) through granular activated carbon (GAC) filtration, followed by final disinfection with sodium hypochlorite prior to distribution. Four DWTPs, monitored in deliverable D2.5, are the focus of the integrated risk assessment application: Assiano, Chiusabella, Feltre and San Siro DWTPs. The main focus was on the effect of disinfection, sampling before and after disinfection (Figure 13).

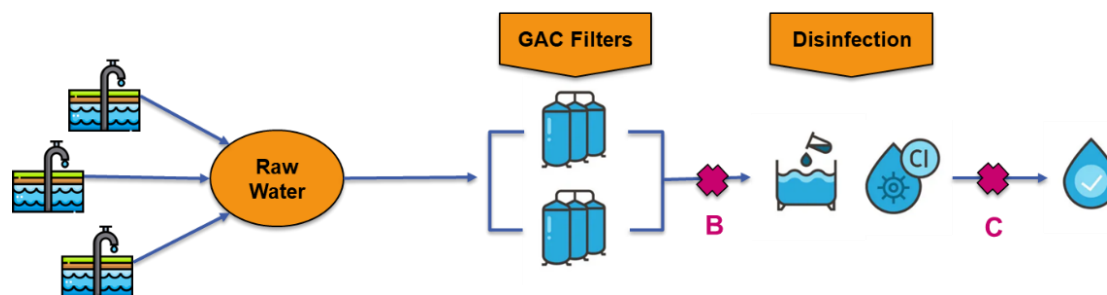


Figure 13: Treatment train and sampling points for the four monitored DWTPs.

Monitoring campaign for microbial and chemical water characterization

The monitoring campaign was performed in 2024 and 2025: Assiano was sampled in two periods (5th July–30th August 2024 before GAC installation, and 16th September–8th November 2024 after, with ~15% of flow through GAC); Chiusabella (5th July 2024–23rd May 2025) had ~50% flow through GAC filters; Feltre (5th July 2024–20th June 2025) included GAC regeneration from 18th November 2024 to 14th January 2025; San Siro was sampled over the same period as Feltre.

Samples were collected every two weeks and, in each sampling point, the following analyses were performed: i) NOM characterization through Total Organic carbon/Dissolved Organic carbon (TOC/DOC), UV/VIS absorbance and fluorescence measurements; ii) microbiological characterization: THB, *Escherichia coli*, *Pseudomonas aeruginosa*, and total cell count through lab cytometric analysis; iii) regulated and unregulated DBPs, specifically THMs and polar sulphonated DBPs; iv) EBM analyses through in vitro CALUX bioassays.

Case Study Specific QMRA, QCRA and EBM input parameters

Statistical distributions of the concentrations of each parameter were built from monitoring data. To deal with censored data, namely data below the analytical instrument Limit of Detection (LOD), the maximum likelihood method for left-censored data (MLE_{LC}) was applied (Cantoni et al., 2021). For each parameter and sampling point, fits to the lognormal, normal, Weibull, gamma, Poisson and logistic statistical distributions were tested. The data fitting to specific distributions were performed with the `fitdistr` function for MLE_{LC} in the R `fitdistrplus` package (Delignette-Muller et al., 2010). The model selection was based on the log-likelihood criterion: the distribution with the maximum log-likelihood were chosen as the most appropriate method (Myung, 2004). 95-percent confidence intervals for the distribution parameters and summary statistics were calculated via non-parametric bootstrapping (1000 iterations) with the `bootdiscens` function in the R `fitdistrplus` package (Rodríguez-Gil et al., 2018).



3. Results

This section presents the outcomes of the development of an integrated risk assessment framework and three different applications of the framework in three case studies monitored in the project.

3.1. Developed integrated risk assessment framework

The developed integrated risk assessment framework is schemed in Figures 14-17. In developing the integrated risk assessment framework, the first decision tree (Figure 14) defines a structured procedure to identify the most appropriate level and type of risk assessment based on the availability and robustness of exposure data. The process begins with the verification of whether exposure data is available. In the absence of exposure data, the framework directs the assessment toward a semi-quantitative approach, such as risk matrices supported by expert judgment, ensuring that risk management decisions can still be informed even under severe data limitations.

When exposure data is available, the next decision step concerns data numerosity. If the dataset is limited, a deterministic risk assessment based on point-value estimates is recommended. Conversely, when sufficient data is available, the framework supports a fully quantitative probabilistic risk assessment, explicitly incorporating variability and uncertainty in exposure and hazard characterization.

Once the quantitative level is defined, the selection of the specific risk assessment methodology depends on the type of data available. If only microbial indicators or pathogen concentrations are measured, the framework directs the analysis toward Quantitative Microbial Risk Assessment (QMRA). If only disinfection by-product (DBP) concentrations are available, Quantitative Chemical Risk Assessment (QCRA) is performed. If only effect-based monitoring (EBM) data are available, a quantitative assessment based on bioanalytical responses is conducted. When multiple data streams are available, combined assessments are implemented. When all three datasets are available, a fully integrated microbial, chemical, and EBM risk assessment is performed, according to the framework described in Figures 15 to 17. When only two data sources are available, the framework can be applied as it described in the case of full availability of data neglecting the part of the framework for which data are not available.

In the following sections, the application of this framework is demonstrated through three case studies that, as shown in Figure 14, are characterized by different levels and combinations of available data, thereby illustrating its flexibility and scalability across diverse monitoring scenarios.

The proposed integrated framework (separated in Figure 15, 16 and 17 for better visualization) combines Quantitative Microbial Risk Assessment (QMRA), Quantitative Chemical Risk Assessment (QCRA), and Effect-Based Monitoring (EBM) into a unified, probabilistic approach for health-based evaluation of drinking water disinfection. The framework is designed to consistently assess microbial risk reduction and chemical risk formation within a common metric, while incorporating bioanalytical evidence to address mixture toxicity and data gaps.

The assessment begins with the exposure assessment step (Figure 15), through the characterization of microbial indicators and pathogens, disinfection by-products (DBPs), and bioanalytical responses measured at the inlet and outlet of the disinfection process. For each component, probability distributions are fitted to concentration data in order to explicitly account for variability and uncertainty.



In the **QMRA branch**, being a well-established procedure, both for the hazard assessment and risk assessment steps (Figures 15 and 16) standard procedures are proposed: pathogen concentration distributions before and after disinfection are used to derive removal efficiencies and to estimate infection probabilities, which are subsequently translated into Disability-Adjusted Life Years (DALYs). This results in a probabilistic distribution of microbial health burden associated with the treatment configuration.

In parallel, the **QCRA branch** models DBP concentration distributions at the same sampling points and derives formation patterns across the disinfection step. Exposure assessment and toxicity characterization are then combined to estimate chemical risk. A central element of the framework is the harmonization of chemical risk with microbial risk through conversion into DALYs. When compound-specific DALY values are available, they are directly used to construct DALY distributions for individual DBPs. When health-based values exist only for a limited number of compounds within a class, relative potency approaches are applied to extend toxicity estimates to structurally or toxicologically similar DBPs. In the absence of toxicological data, quantitative structure–activity relationship (QSAR) models are used to estimate toxicity parameters and derive corresponding DALY contributions. In this way, chemical risk formation is expressed as a probabilistic DALY distribution comparable to the microbial burden.

Effect-Based Monitoring constitutes an independent yet complementary line of evidence within the framework. Bioanalytical equivalent concentrations are fitted before and after disinfection, and changes in biological response are quantified. Measured responses are compared with Effect-Based Trigger (EBT) values to determine the probability of exceedance and to identify potential mixture toxicity not captured by targeted chemical analysis. Beyond its screening function, EBM supports the estimation of relative toxic potency for insufficiently characterized DBPs and provides a consistency check between chemically derived DALY estimates and observed biological effects.

The risk assessment stage (Figure 17) integrates the microbial DALY reduction and the chemical DALY formation across the disinfection process. A coherence analysis evaluates whether variations in chemical DALY are consistent with observed EBM responses. Agreement between these lines of evidence increases confidence in the chemical risk estimates, whereas discrepancies indicate the potential presence of unknown or insufficiently characterized toxicants requiring further investigation. The final step consists of summing microbial and chemical DALY contributions to obtain a combined health risk metric, thereby enabling explicit quantification of the trade-off between pathogen inactivation and by-product formation.

Overall, the framework provides a structured and transparent methodology to integrate acute microbial risk, chronic chemical risk, and mixture-related biological effects within a single health-based metric. By harmonizing methodologies and incorporating probabilistic uncertainty analysis, it supports risk-informed optimization of disinfection practices and strengthens decision-making in drinking water management.



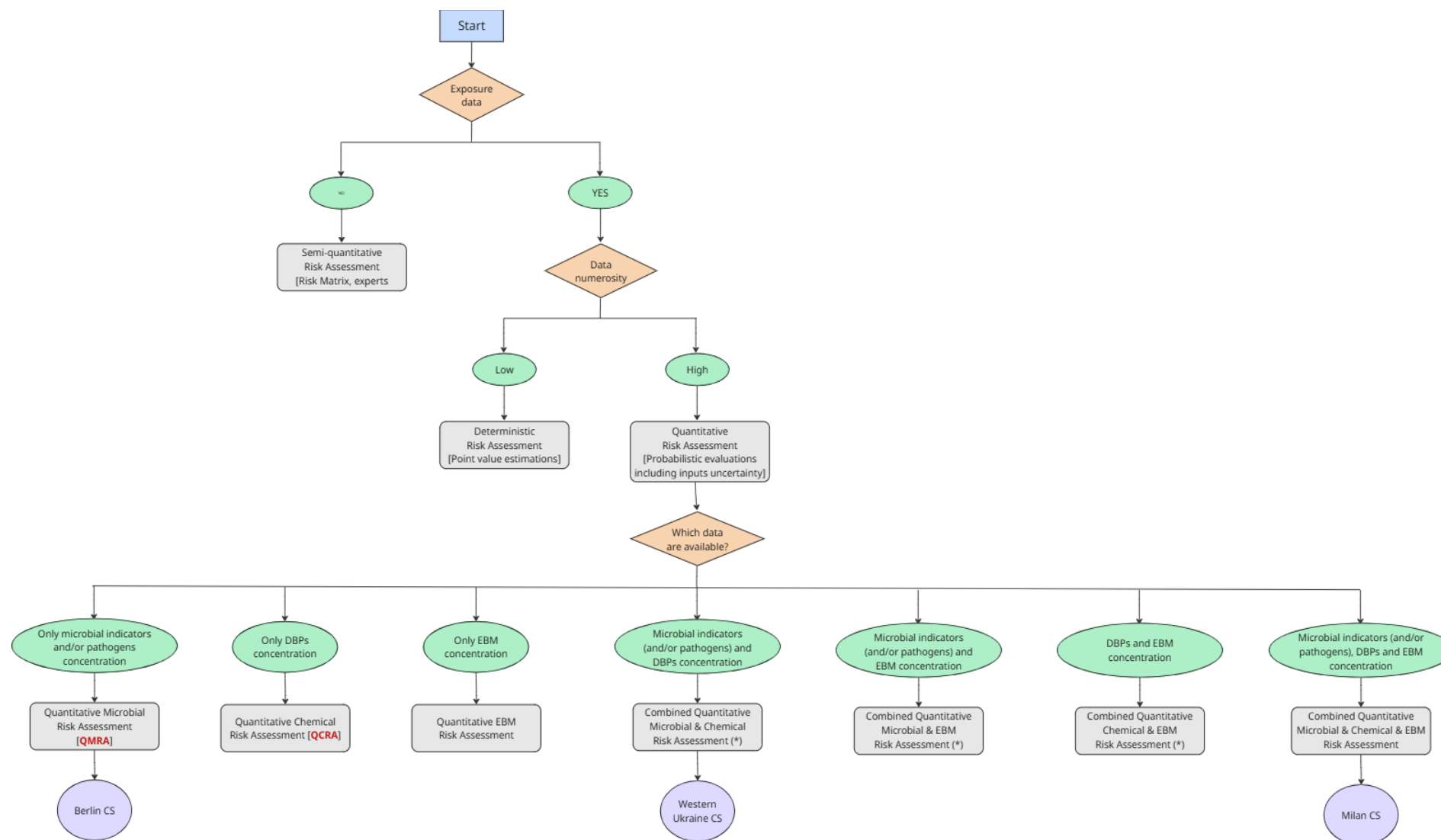


Figure 14: Decision tree supporting the integrated risk assessment framework to be applied based on the available data for the analysed case study.

This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101081980.

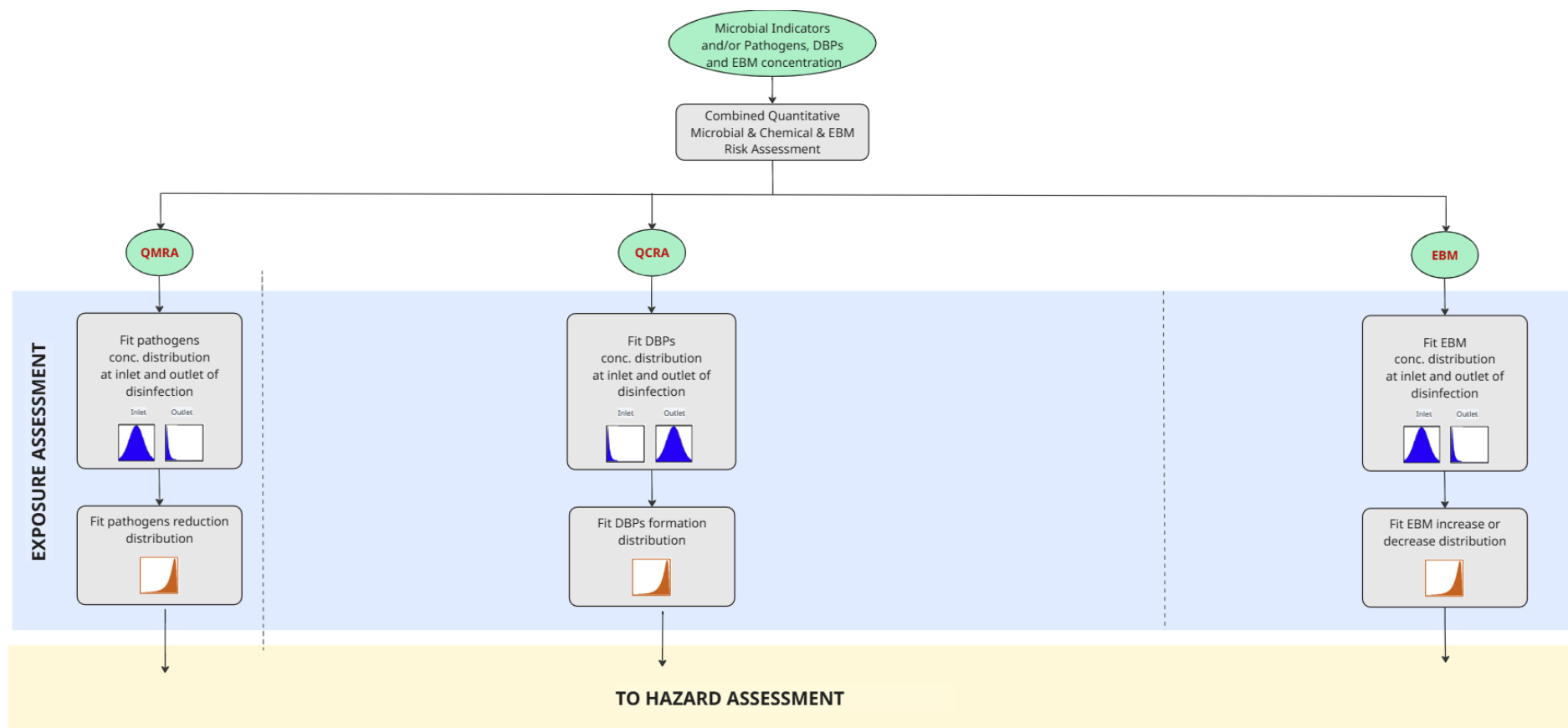


Figure 15: First step (Exposure assessment) of the integrated risk assessment framework combining QMRA, QCRA and EBM methodologies.

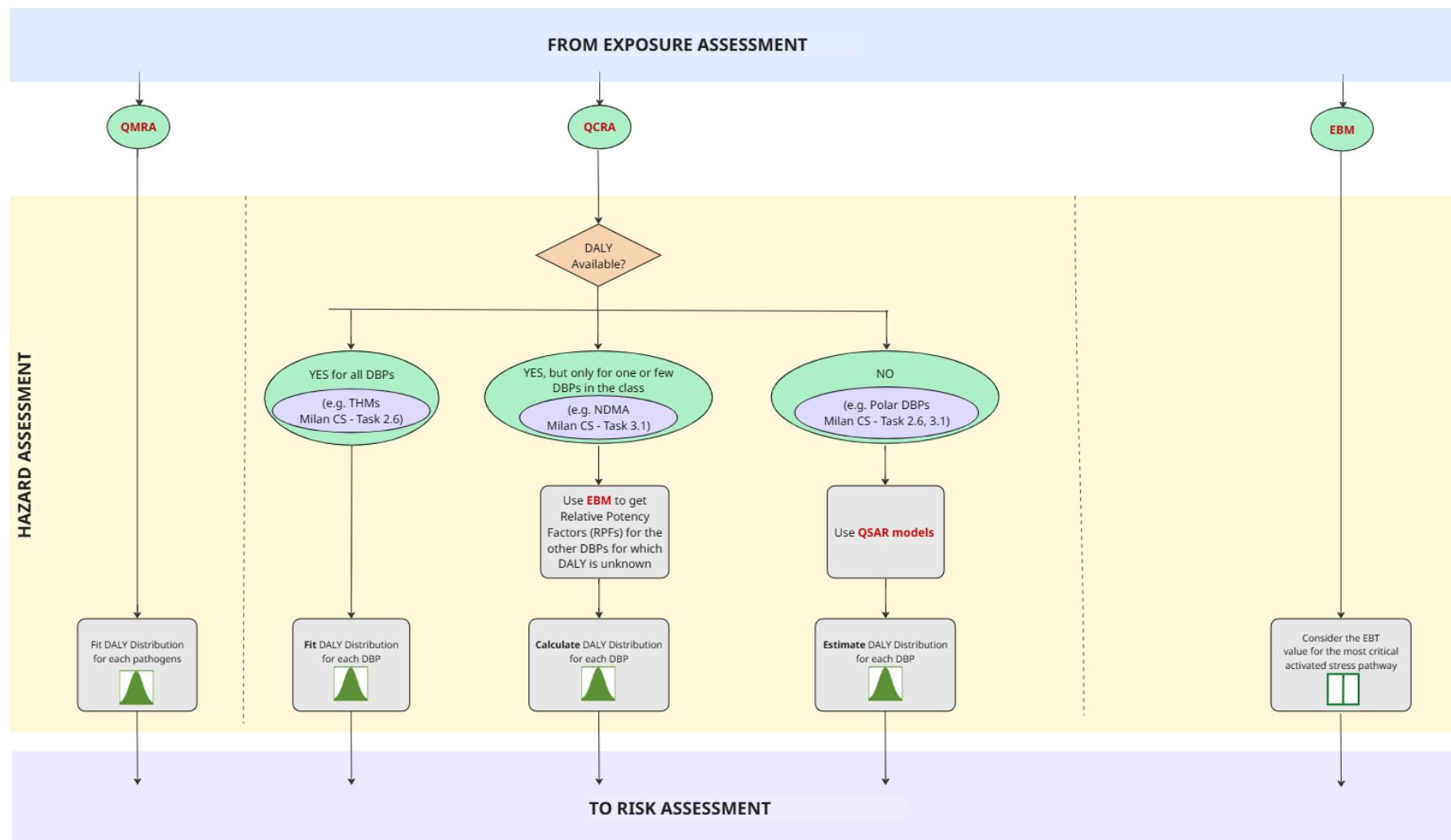


Figure 16: Second step (Hazard assessment) of the integrated risk assessment framework combining QMRA, QCRA and EBM methodologies.

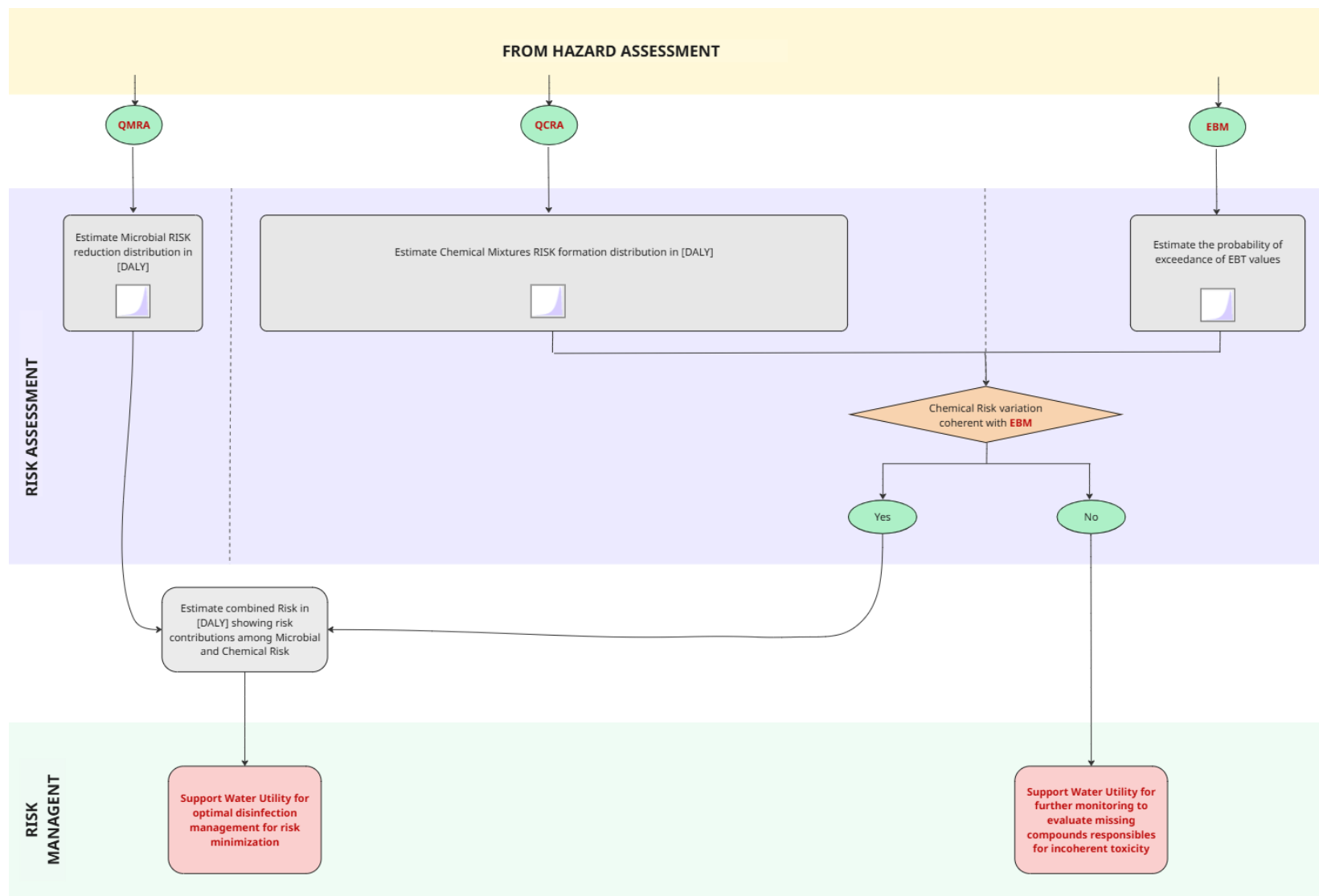


Figure 17: Third step (Hazard assessment) of the integrated risk assessment framework combining QMRA, QCRA and EBM methodologies.

This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101081980.

3.2. Framework application to CS#1 Berlin, Germany

Specific goals of the framework application

The verification of infectious-hygiene safety in drinking water has long relied on the measurement of conventional bacterial indicator organisms. Historically, the German Drinking Water Ordinance (TrinkwV, 2011) combined mandatory routine and random sampling for parameters such as *E. coli*, coliform bacteria, and enterococci. This methodology has been effective for decades, successfully mitigating the risk of major water-associated diseases including cholera, typhoid fever, shigella dysentery, and hepatitis A. However, contemporary regulatory frameworks are shifting towards a more comprehensive, proactive safety paradigm. The TrinkwV (2023) moved beyond random sampling to integrate a risk-based management approach. Advances in microbiological analytics and epidemiology, as well as the scientific investigation of epidemic outbreaks of disease have shown that not all pathogens are reliably detected. These include in particular some viruses (Wielen et al., 2008) as well as permanent parasite forms (*cryptosporidia* and *giardia*). These waterborne pathogens can be infectious even in low concentrations in drinking water and are more resistant to environmental stress and technical disinfection (e.g. chlorination) than bacterial indicator organisms. In order to detect these low concentrations in drinking water, testing of these pathogens would have to be carried out in very large volumes of water. This is not possible by conventional analytical methods. To overcome the analytical constraints associated with detecting pathogens in large water volumes, this study utilizes ultrafiltration-based microbial enrichment (see section 2.2.1). This concentration technique enables the detection of low-level microbial indicator that are otherwise invisible to routine monitoring. By integrating this data into a QMRA framework, the study provides an evaluation of infectious risks, supporting the evidence-based safety requirements mandated by TrinkwV (2023).

In this study, a QMRA is applied to a managed aquifer recharge (MAR) site. At the waterworks in Berlin-Spandau deliberate groundwater recharge is necessary because natural recharge does not meet the water demand. The source water for this groundwater recharge is abstracted from the Havel River and pre-treated prior to recharge. Havel River water is pre-treated via flocculation and rapid sand filtration to remove suspended solids and nutrients prior to groundwater recharge. The QMRA focused on the subsurface passage as the primary hygienic barrier, a critical component in site-specific risk management where natural attenuation replaces or supplements technical treatment steps. Technical post-treatment was not taken into account, since the subsurface is the most important barrier for the retention of pathogens at this site. The primary objectives of this study are to:

1. Quantify the hygienic barrier value of the subsurface for specific pathogens to determine its natural log-reduction capacity
2. Conduct a site-specific QMRA to evaluate the human health risks associated with the recovered groundwater



Results of framework application

In particular, this study applied QMRA to evaluate the influence of hydraulic residence time (HRT) on health-based risk metrics, expressed as disability-adjusted life years (DALYs) and infection probability.

Across all pathogen groups and both risk metrics, increasing hydraulic residence time results in a reduction in health risk, reflecting enhanced pathogen attenuation with longer residence time (Figure 18).

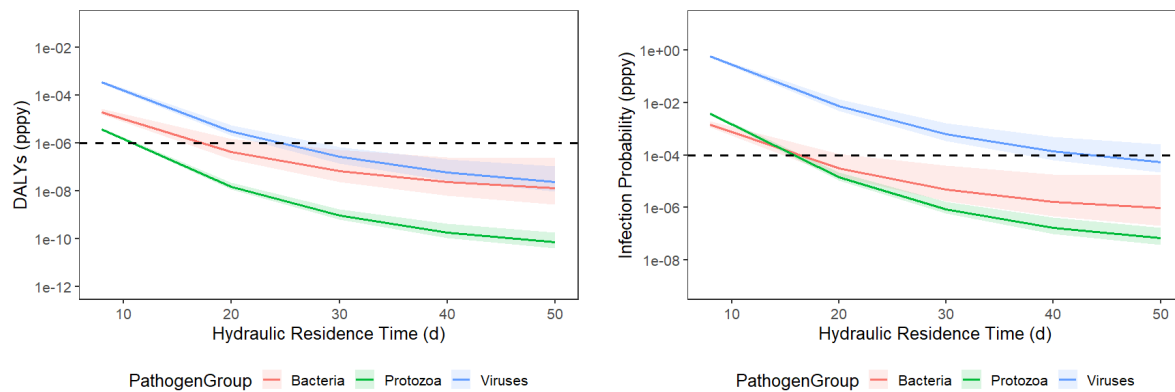


Figure 18: Health-based risk metrics as a function of hydraulic residence time (HRT). DALYs (left) and infection probabilities (right) are shown for bacteria, viruses, and protozoa. Solid lines represent median estimates, while shaded envelopes denote uncertainty derived from Monte Carlo simulations: ± 1 standard deviation. The dashed horizontal lines indicate health-based targets of 10^{-6} DALYs per person per year (pppy) and 10^{-4} infection probability pppy, respectively.

A pronounced initial decline in risk at lower HRTs indicates high efficiency in early-stage removal and diminishing removal at longer residence times. This asymptotic behaviour is a direct consequence of the cap-limit log-removal model.

The health-based risks of protozoa are found to be below the risk metrics after approximately 12 and 19 days of HRT for the tolerable burden of disease and the probability of infection, respectively. This is due to the relatively high LRV in the subsurface (3.33 ± 0.40 at 8 days HRT), the low probability of *Cryptosporidium parvum* oocysts occurring in source water, and the associated low dose-response relationship and infection probability.

In contrast to protozoan pathogens, the health-based risks of bacterial pathogens are found to be below the tolerable burden of disease (10^{-6} DALYs per person per year) after approximately 30 days of hydraulic retention time (HRT) and are associated with greater uncertainty. Although the calculated LRV in the subsurface (3.07 ± 0.64 at 8 days HRT) is similar to that of protozoan removal, the higher occurrence in source water and the more pronounced dose-response relationship mean that bacteria pose a higher microbial risk. Nevertheless, an HRT of 30 days in the subsurface is sufficient to meet both health-based risk metrics.

Although median health-based metrics at an HRT of 50 days comply with health-based thresholds, the upper bounds of uncertainty for viral infection probability remain above the tolerable threshold. This behaviour is explained by the comparatively low LRV for viruses in the subsurface (2.87 ± 0.45 at 8 days HRT), which is the lowest among the pathogen groups considered. Although the applied LRV must be considered as a minimum LRV, reduced attenuation efficiency implies that a greater fraction of viruses remains active even after residence times of 50 days. Moreover, viruses pose a disproportionate risk to human health due to their steep dose-response relationships and low infectious doses.



Limitations

Inflow concentrations and distributions of pathogenic microorganisms were not measured directly but were instead inferred using literature derived pathogen-to-indicator ratios applied to site-specific indicator measurements (bacteria and viruses), or were adopted directly from published monitoring data in the absence of local measurements (protozoa). While this approach is common in QMRA where direct pathogen monitoring is impractical, it introduces substantial uncertainty because relationships between indicators and pathogens are highly variable and often site-specific. Pathogen occurrence in surface waters is known to vary over several orders of magnitude in response to temporal and spatial factors, including upstream wastewater discharges, rainfall events, seasonality, and catchment characteristics. Consequently, the constructed inflow pathogen distributions should be interpreted as conservative, but approximate representations of potential source water quality rather than precise measurements of true pathogen occurrence.

Due to a lack of positive detection in groundwater, it was not possible to assess the transport of viruses in the subsurface by measurements. Consequently, the applied LRV of viruses is considered to be the minimum removal value, meaning that the actual attenuation capacity of the subsurface is likely to be somewhat higher. However, as even small residual concentrations of viruses can pose significant health risks, the impact of uncertainty in removal efficiency and exposure assumptions is amplified. From a risk management perspective, the results emphasise the need for additional validation measures to reduce uncertainty. Several studies have suggested using pepper mild mottle virus (PMMoV) as a viral tracer for human faecal contamination and for the removal of enteric viruses in water treatment (Kitajima et al., 2018) and MAR systems (Betancourt et al., 2014). As PMMoV is often present in high concentrations, it appears to be ideal for testing the removal of enteric viruses (Symonds et al., 2019). Monitoring of PMMoV is therefore recommended to be included in future microbial risk assessments.

The QMRA was only carried out for one well with a relatively short HRT. However, the raw water at the waterworks is a mixture from 44 wells, most of which have a much longer HRT and are less affected by surface water. Consequently, the overall risk at the Berlin-Spandau waterworks is much lower.



3.3. Framework application to CS#4 Western Ukraine

Specific goals of the framework application

In the Western Ukraine case study, following abstraction, the bank-filtered water is subjected to post-treatment consisting of disinfection using sodium hypochlorite. Disinfection is implemented to ensure microbiological safety and compliance with drinking water quality standards, particularly during periods of elevated river discharge or flooding when pathogen loads in surface water may increase. For this reason, in Western Ukraine case study the focus of the monitoring and risk assessment is both related to microbial parameters (*E. coli*) and chemical DBPs typically formed with sodium hypochlorite disinfection, namely THMs. Data on EBT are not available for this case study as the monitoring did not cover such measurements. therefore, this is a case in which both QMRA and QCRA are applied to quantify health-based risk metrics, expressed as disability-adjusted life years (DALYs) and infection probability. This will be useful to evaluate the effect of both riverbank filtration and chemical disinfection in ensuring water safety at the consumer.

The QMRA applications for Berlin and Western Ukraine both focus on the subsurface passage, but they differ significantly in terms of data availability. A fundamental limitation in conducting pathogen-specific QMRA at RBF sites is the scarcity of comprehensive microbial data. Pathogen monitoring, particularly for viruses (e.g., norovirus, adenovirus) and protozoa (e.g., *Cryptosporidium*, *Giardia*), is technically challenging, resource-intensive, and often subject to high detection limits and analytical variability. Consequently, datasets for these pathogens are frequently incomplete or entirely absent. In contrast, long-term monitoring data for faecal indicator organisms such as *E. coli* are more readily available due to the simplicity, low cost, and robustness of culture-based methods. The relevance of *E. coli* measurements in this context lies in their ability to reflect both the effectiveness of microbial attenuation and the hydraulic connectivity between the river and the abstraction wells. By monitoring *E. coli* in both surface water and post-filtration well water, it is possible to quantify log removal values and evaluate seasonal variations in microbial quality. Consequently, *E. coli*-based QMRA at RBF sites provides valuable insights into relative risk reduction and system performance, even in the absence of pathogen-specific measurements. While this approach does not capture the complete spectrum of microbial risk, it serves as a scientifically defensible tool for screening and comparative assessments, particularly when integrated with uncertainty analysis and conservative risk assumptions. Therefore, this study presents a screening-level or proxy-based QMRA, rather than a full pathogen-specific risk assessment.



Results of framework application

As for the QMRA, the applied median inflow concentration (organism/L) and median log reduction are shown in Figure 19.

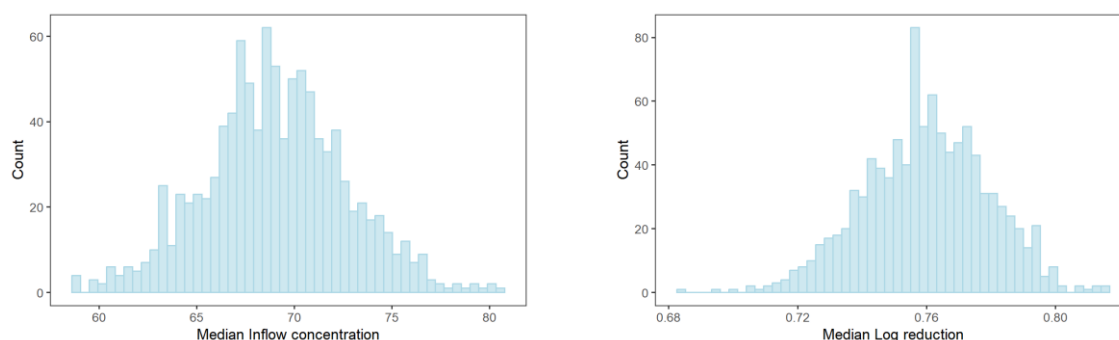


Figure 19: Histograms of median inflow concentration of bacteria (organism/L in source water) and median log reduction in subsurface.

The *E. coli* inflow concentration is estimated from the negative binomial model fitted to the sampling data from the surface water. A uniform distribution was subsequently applied to the source water inflow. This stochastic approach assigns an equal probability to all values within the defined intervals (0-138 organism/L; see Table 3), providing a conservative baseline for the assessment. As illustrated in Figure 20, elevated health risks are associated with the riverbank filtration process alone, where high bacterial inflow concentrations are not sufficiently attenuated by the low LRV of the subsurface.

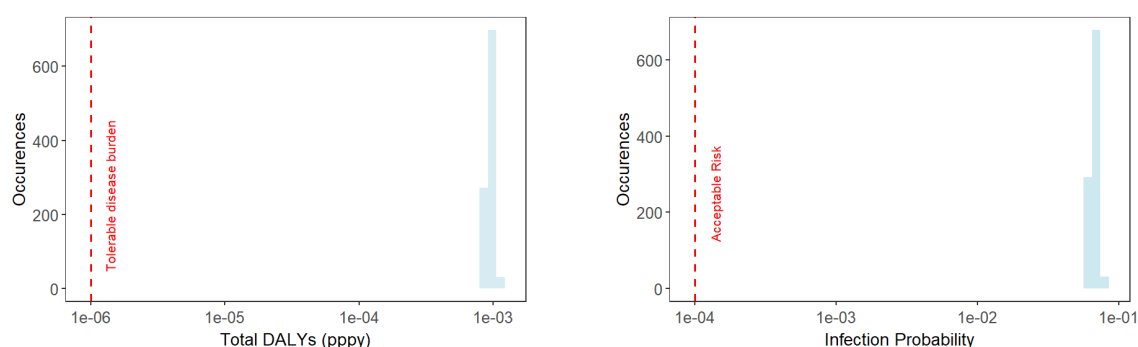


Figure 20: Health-based risk in DALYs (left) and infection probabilities (right) for bacteria. The dashed vertical lines indicate health-based targets of 10^{-6} DALYs per person per year (pppy) and 10^{-4} infection probability pppy, respectively.

The QMRA results indicate that current raw water microbial levels exceed the acceptable health-based targets of 10^{-6} DALYs per person per year and 10^{-4} infection probability per person per year by several orders of magnitude. The site-specific log removal value (LRV) for bacterial transport (0.78 ± 0.29 at an HRT of 32.5 days) is low given the residence time, likely due to the high permeability of the alluvial aquifer, the shallow depth of the abstraction wells (~ 29 m below ground level), and the short nominal distance between the wells and the riverbanks. These risks may be further exacerbated during periods of elevated river discharge or flooding, when pathogen concentrations in surface water are expected to increase. Consequently, following abstraction, the bank-filtered water is subject to post-treatment disinfection using sodium hypochlorite. QMRA-derived health-based risk metrics including the whole treatment chain from the source water (surface water), riverbank filtration and disinfection is shown in Figure 21.



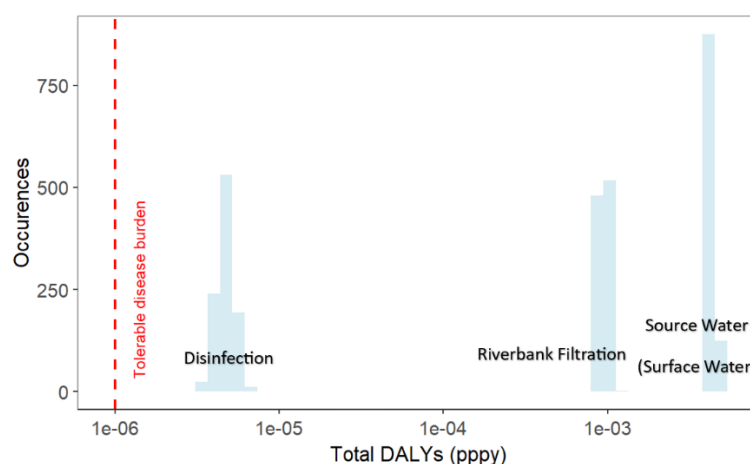


Figure 21: Health-based risk reduction of treatment chain in DALYs for bacteria in the source water (surface water), after riverbank filtration and after chemical disinfection. The dashed vertical line indicates health-based targets of 10^{-6} DALYs per person per year (pppy).

Disinfection was modeled using a uniform distribution with an LRV range of 2 to 6 log units. Despite this addition, the complete treatment chain failed to achieve the health-based target of 10^{-6} DALYs per person per year (pppy).

However, this step forms chemical DBPs such as trihalomethanes, that are responsible for chemical risk. Moreover, since the residual disinfectant that remains in the disinfected water can react with residual organic matter along the drinking water distribution network (DWDN), further formation of THMs can happen in the DWDN. The fate of THMs from the source water until points in the DWDN is shown in Figure 22.

The results presented in Fig. 22 show a clear evolution of trihalomethane (THM) concentrations from the source water to the different points of the drinking water distribution network (DWDN). In the raw source water, THMs were already detectable, with chloroform (TCM) being the dominant species, reaching concentrations in the order of 2–3 $\mu\text{g/L}$, while brominated THMs (BDCM, DBCM, and TBM) were present at lower levels. Following riverbank filtration (RBF), a substantial reduction of all THM species was observed at both monitoring points, with concentrations approaching zero or remaining at trace levels. This indicates that the RBF system effectively attenuates pre-existing THMs, likely due to a combination of dilution, volatilization, and biodegradation processes within the aquifer.

After sodium hypochlorite disinfection, a marked increase in THM concentrations was detected, confirming the formation of disinfection by-products as a consequence of the reaction between free chlorine and residual natural organic matter (NOM). At this stage, both chloroform and brominated species increased, with DBCM and BDCM showing notable formation, indicating the presence of bromide in the raw water and its incorporation into THMs during chlorination. Chloroform remained one of the predominant species, but the relative contribution of brominated THMs increased compared to the source water.



Within the DWDN, further spatial variability in THM concentrations was observed across the five sampling points. In general, total THM concentrations tended to increase at several downstream locations compared to the post-disinfection point, highlighting ongoing formation driven by residual disinfectant and remaining reactive organic precursors. In particular, some network points exhibited elevated levels of DBCM and BDCM, suggesting that brominated species become increasingly relevant along the distribution system. TBM was consistently detected at lower concentrations but followed the same increasing trend at selected points. The variability among DWDN locations likely reflects differences in water age, hydraulic conditions, temperature, and local NOM reactivity.

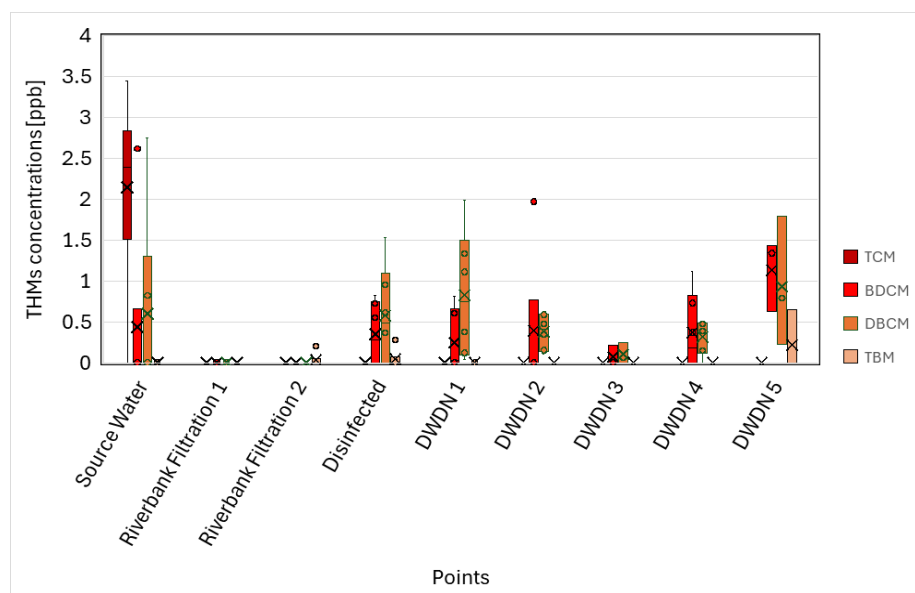


Figure 22: Concentration of four trihalomethanes in the source water, after riverbank filtration, after chemical disinfection and in 5 points along the DWDN. TCM: Chloroform; BDCM: Bromodichloromethane; DBCM: Dibromochloromethane; TBM: Bromoform.

To place the concentration data in a public health perspective and enable a direct comparison between microbial and chemical hazards, the measured levels were translated into disability-adjusted life years (DALYs) per person per year. Expressing both QMRA and QCRA outcomes in the same health-based metric allows the relative magnitude of microbial and chemical risks to be assessed against common health targets (e.g., 10^{-6} DALYs pppy) and supports balanced risk management decisions. As shown in Figure 23, the microbial risk in the source water largely exceeds the health-based target by several orders of magnitude, confirming the urgent need for effective treatment. Riverbank filtration substantially reduces the microbial DALY, yet residual risk remains above the acceptable benchmark, justifying the subsequent disinfection step.

In contrast, the chemical risk associated with THM exposure, expressed as DALYs derived from QCRA, remains several orders of magnitude lower than the corresponding microbial risk across all treatment stages. Even after disinfection, where THM formation increases, the estimated chemical risk overcome the microbial one but it remains comparatively low and close to or below the health-based reference value. This side-by-side representation highlights that, within the studied system, microbiological risk is the dominant driver in raw and bank-filtered water, whereas chemical risk becomes relevant primarily after chlorination but does not outweigh the public health benefit achieved through pathogen inactivation. In fact, even after disinfection, the DALYs associated with THMs remain well below the microbial risk observed in untreated water.



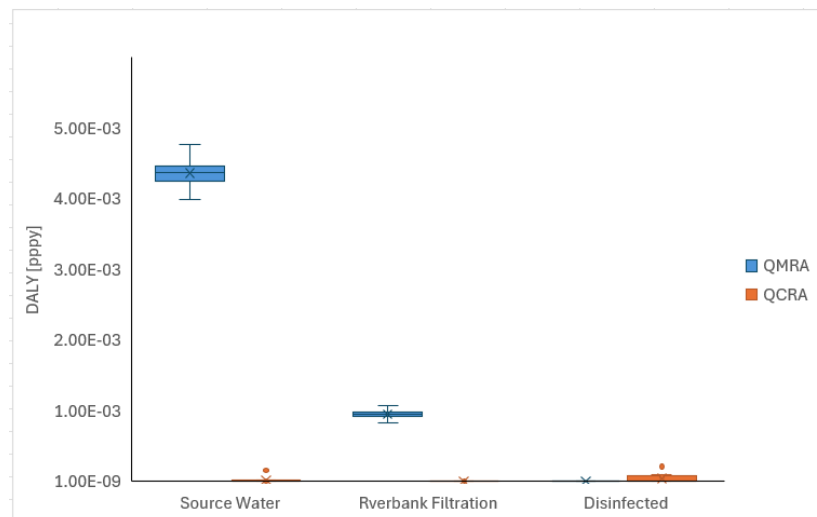


Figure 23: Health-based risk in DALYs for microbial and chemical risks in the source water, after riverbank filtration and after chemical disinfection.

Overall, the results confirm that while post-abstraction chlorination is essential to achieve the microbiological safety targets identified by the QMRA, it also leads to the formation and further evolution of THMs along the distribution system. This highlights the need for an integrated risk-based management approach that simultaneously considers microbial and chemical risks, optimizes disinfectant dosing, and controls precursor removal to limit DBP formation while maintaining adequate residual protection throughout the network. Presenting both risk types in DALYs therefore provides a transparent and quantitative basis for evaluating trade-offs between microbial safety and DBP formation within a risk-based management framework.



3.4. Framework application to CS#2 Milan, Italy

Specific goals of the framework application

The Milan metropolitan area provides a relevant and representative context for testing integrated, risk-based approaches to drinking water safety management. Drinking water is abstracted from groundwater sources and treated through granular activated carbon (GAC) filtration, followed by final disinfection with sodium hypochlorite prior to distribution. This treatment configuration is designed to balance effective removal of organic micropollutants and microbial contaminants with the need to maintain a disinfectant residual in the distribution network. However, as with many chlorination-based systems, the process involves a potential trade-off between microbiological safety and the formation of DBPs, particularly THMs.

For this case study, comprehensive datasets are available from four DWTPs characterized by different raw water qualities and distinct microbial and chemical profiles. The dataset includes: (i) microbial contamination indicators to support QMRA; (ii) concentrations of regulated and relevant DBPs, with specific focus on THMs, to enable QCRA; and (iii) EBM results derived from bioassays, providing integrative information on the overall biological activity of treated water. The coexistence of these three lines of evidence offers a unique opportunity to evaluate drinking water safety through complementary and potentially synergistic assessment tools.

The objective of the Milan case study is to apply and test an integrated health risk assessment framework combining QMRA, QCRA, and EBM to four full-scale drinking water treatment plants with differing characteristics. Specifically, the study aims to compare and integrate the outputs of these three approaches within a common risk-based framework, expressed in comparable health metrics where possible. Through this integrated application, the Milan case study aims to demonstrate the feasibility and added value of combining QMRA, QCRA, and EBM to support holistic, evidence-based decision-making in drinking water treatment and to move beyond single-hazard or single-metric evaluations toward a comprehensive public health protection strategy.

Results of framework application

Starting from the exposure step of the framework (Figure 15), an overview of the measured concentrations of bacteria, THMs and EBM, in the four DWTPs before and after disinfection is provided (Figure 24). Looking at the characteristics of the water entering the disinfection phase in the four DWTPs, the highest microbial load is found in Assiano and Chiusabella, while Feltre and San Siro DWTPs have low microbial contamination. Trihalomethanes are found also in the raw water at these DWTPs: San Siro has the highest inlet concentration (median of 6.1 µg/L and reaching a maximum of 8.3 µg/L), while the other three DWTPs show limited THMs concentration ranging between 0.3 and 1.7 µg/L.

Given these characteristics we can state that the four DWTPs cover a wide range of input characteristics and provide a good example of several scenarios with different microbial and chemical quality.



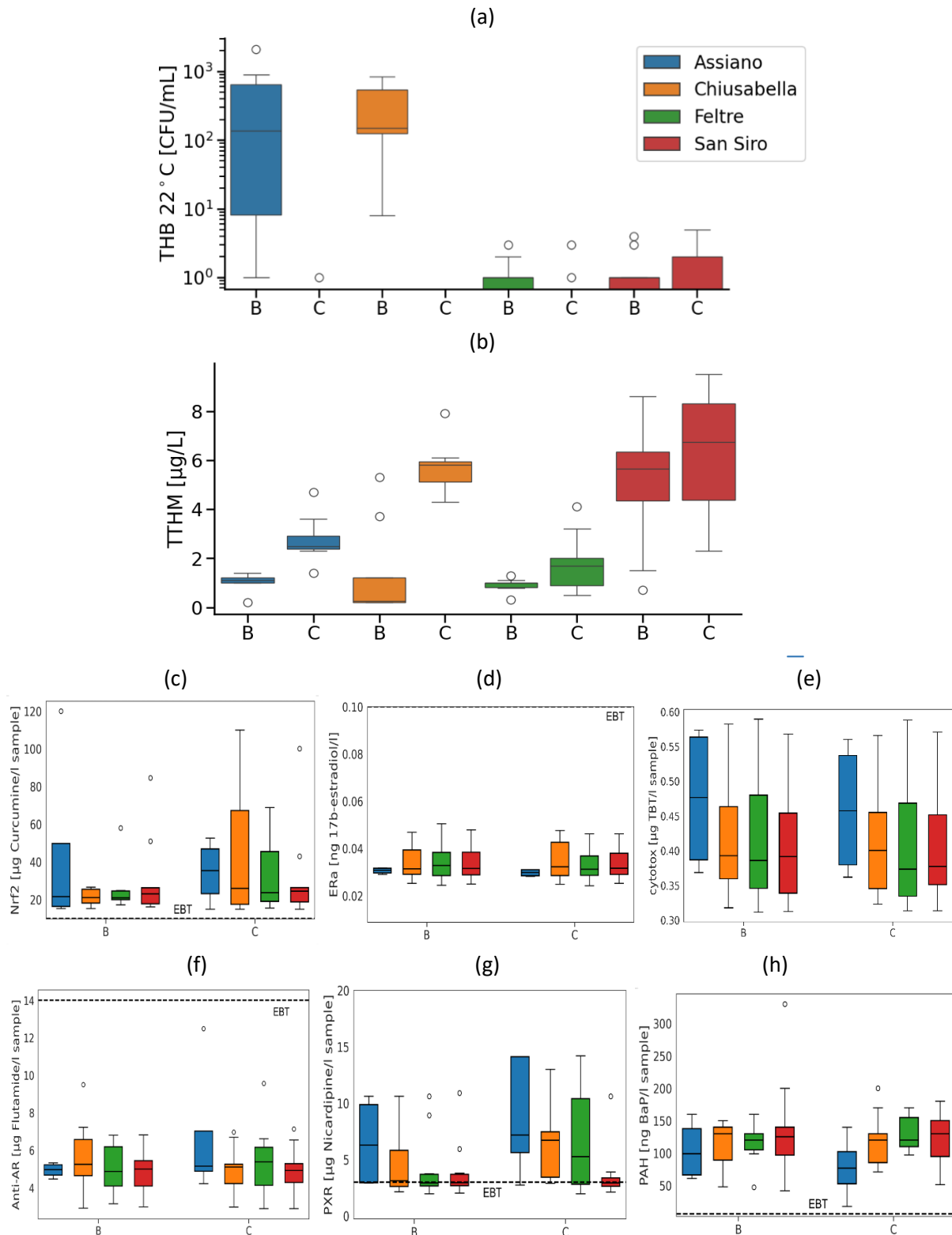


Figure 24: Concentration of (a) bacteria, (b) Total Trihalomethanes (TTHMs) and (c-h) EBM for different endpoints in the four DWTPs at the inlet (Point B) and outlet (Point C) of the disinfection phase.



Moving to the hazard assessment step of the framework (Figure 16), the DALY approach is applied without need for estimating the relative potency factors through EBM or QSAR models as the DALY calculation is available from previous studies for all the four THMs.

Finally, for the risk assessment step, first the chemical risk is compared to the EBM analyses to evaluate whether these two are consistent. Since we are focusing the chemical risk assessment on trihalomethanes, we have first to evaluate which of the endpoints analysed in the bioassay tests should be used as a comparison. For this, EBM on synthetic solutions of single target compounds have been used to assess which of the endpoint show activity in the presence of trihalomethanes (Figure 25).

Figure 25: EBM results of target compounds for the analysed bioassays.

compound	Cytotox20%	ERa	AR-ant	PXR	AR	Nrf2	p53 GENTOX
Assay-specific reference	-6.6	-12.2	-7.7	-7.1	-12.3	-5.4	-9.0
chloroform	>-3	>-4	>-4	>-4	>-3	>-3	>-3
chlorodibromomethane	>-3	>-4	>-4	>-4	>-3	>-3	>-3
bromoform	>-3	-4.2	>-4	>-4	>-3	-3.4	>-3
iodoform	-3.4	>-4	>-4	>-4	>-3	>-3	>-3
dichloroacetonitrile	-3.5	>-4	>-4	>-4	>-3	-3.5	-3.6
chloroacetic acid	>-3	>-4	>-4	>-4	>-3	-4.0	-3.0
bromoacetic acid	-5.0	>-4	>-4	-5.5	>-3	-7.0	-5.6
dichloroacetic acid	>-3	>-4	>-4	>-4	>-3	>-3	>-3
dibromoacetic acid	>-3	>-4	>-4	>-4	-3.5	>-3	>-3
trichloroacetic acid	>-3	>-4	>-4	>-4	>-3	-3.1	>-3
bromodichloromethane	>-3	>-4	>-4	>-4	>-3	>-3	>-3
n-nitrosodiethylamine	>-3	>-4	>-4	>-4	>-3	>-3	>-3
Sodium chlorite	>-3	>-4	>-4	>-4	>-3	-3.1	>-3
2,4,6-trichlorophenol	-4.1	>-4	>-4	-4.2	>-3	>-3	-3.5
2,4,6-tribromophenol	-4.6	>-4	>-4	-4.2	-3.0	>-3	-4.0
potassium bromate	>-3	>-4	>-4	>-4	>-3	-3.5	-3.3

Figure 25 shows that THMs are correlated to an activity in the ERa and Nrf2 bioassays. Figure 26 compares the distributions of concentrations at the sampling point after disinfection of each detected THM (only TCM and TBM were detected), the associated chemical risk in DALY for the four DWTPs.

Firstly, it can be seen that, while TCM was found at higher concentration (from 1 to 10 ug/L) compared to TBM (below 1.5 ug/L) in all four DWTP, when converting concentrations into risk, the main contribution to the final TTHMs risk is due to TBM, as it has higher toxicity compared to TCM. This is an important output that highlights the necessity to convert concentrations into risk to have a better control of the DWTP operations and to always guarantee a safe drinking water to consumers.

While TTHMs concentrations (Figure 26a) have very diversified ranges at the outlet of the disinfection in the four DWTPs (high for San Siro and Chiusabella, medium for Assiano and low for Feltre), when converting concentration into DALYs (Figure 26b) the final chemical risk does not show significant differences among the four DWTPs. This is coherent with the trend of EBM results found with both the ERa and Nrf2 bioassays (Figures 24c and 24d). Therefore, it can be stated that QCRA and EBM provide coherent results.

(a)



This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101081980.

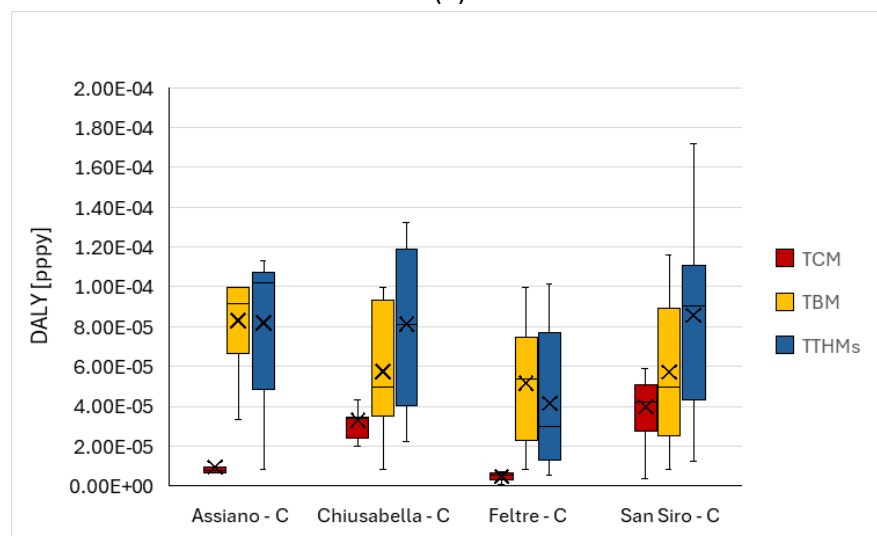
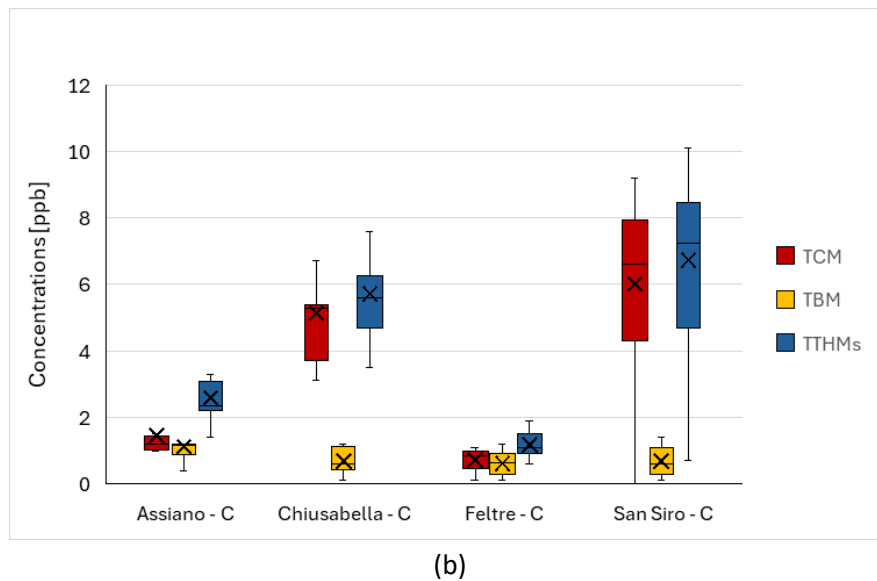


Figure 26: THMs concentrations (a) and chemical risk in DALY (b) for the four monitored DWTPs.

Given the coherence between the QCRA and EBM results, QCRA results are then coupled with the QMRA ones to have an effective quantification of the trade-off generated by the chemical disinfection. To do so, the reduction of microbial risk obtained with the chemical disinfection for all the four DWTPs is compared with the risk generated by the formation of THMs in the process. This differences, defined as $\Delta Risk$ in Figure 27, are both estimated in DALYs and can be directly compared.



Figure 27 illustrates how the reduction of microbial risk is counterbalanced by the simultaneous formation of chemical risk across the four different drinking water treatment plants. In Assiano DWTP, microbial risk decreases substantially, but this benefit is partially offset by the generation of a notable chemical risk, leading to comparable magnitudes of the two risk types. In Chiusabella DWTP the highest variation of both microbial and chemical risk are found. This is probably due to the fact that this DWTP is characterized by the highest microbial load at the entrance of the disinfection phase that is leading to higher doses of chemical disinfectant, with direct consequence on the formation of chemical risk, that dominates the overall risk profile. On the contrary, in both Feltre and San Siro both microbial and chemical risks variations are low, with only slight variations, indicating a balanced and overall low-risk change. Overall, the figure highlights a recurrent pattern: efforts to lower microbial health risks during drinking water treatment can unintentionally increase chemical risks, underscoring the importance of integrated risk evaluation when optimizing treatment processes.

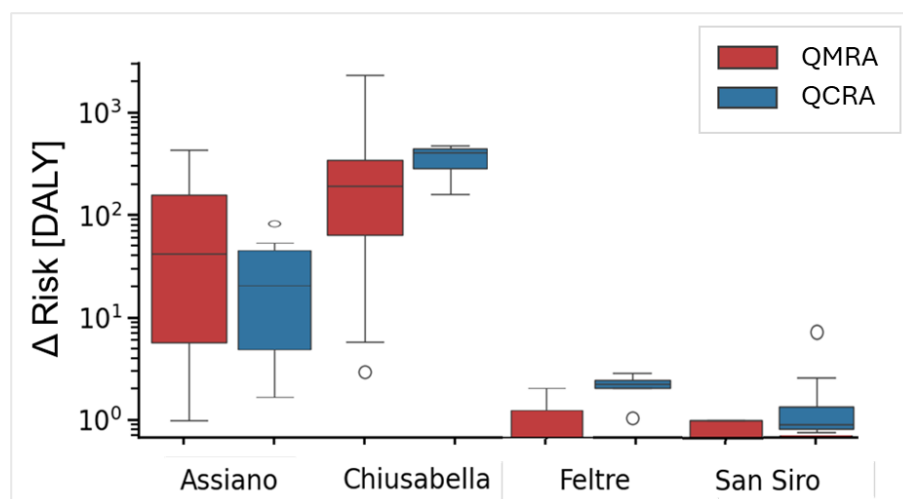


Figure 27: Risk variation (reduction for the microbial risk – in red – and formation for the chemical risk- in blu) expressed in DALY, due to the chemical disinfection in the four DWTPs.



4. Conclusions

This deliverable presents the development and application of an integrated, probabilistic risk assessment framework designed to jointly evaluate microbial, chemical, and effect-based hazards in drinking water systems. The framework responds to the increasing need for holistic, health-based management approaches that acknowledge the complexity of drinking water treatment processes and the trade-offs inherent to chemical disinfection. By merging QMRA, QCRA, and EBM into a unified structure, it provides a coherent method to quantify both acute and chronic health risks and to support optimized decision-making across diverse operational contexts.

The case studies demonstrated the strong influence of local hydrogeological and operational conditions on microbiological safety. In Berlin, the subsurface passage proved to be an effective hygienic barrier, with substantial log-reduction values for bacteria and protozoa and moderate removal of viruses. The application of Bayesian modelling was crucial in appropriately handling left-censored and low-concentration data, and in estimating LRVs with an uncertainty structure that reflects real system behaviour. In contrast, the Western Ukraine riverbank filtration system showed considerably lower LRVs, even at comparable hydraulic residence times, illustrating how aquifer permeability, travel distances, and bank structure strongly affect microbial attenuation. In both cases, the assessment confirmed that relying exclusively on indicator organisms or assumptions about pathogen behaviour may mask system-specific vulnerabilities, and that probabilistic QMRA is essential to transparently reflect uncertainty and to support evidence-based risk management.

In settings where raw or bank-filtered water shows significant microbial loads, as in Ukraine or parts of the Milan system, chlorination is necessary for pathogen inactivation and for maintaining safety throughout the distribution network. However, the analyses also confirmed that chemical disinfection unavoidably generates disinfection by-products, particularly trihalomethanes, whose concentrations may increase further along the network as residual disinfectant reacts with organic precursors. Even though the chemical risks associated with THM exposure were consistently several orders of magnitude lower than the microbial risks in untreated water, they became relevant after disinfection and therefore must be considered in treatment optimization. The DALY-based comparison clearly demonstrated that the health benefits of disinfection far outweigh the chemical risks introduced, but also that unmonitored or poorly controlled precursor levels can lead to unnecessary chemical risk formation and should therefore be managed proactively.

The Milan case study demonstrated the added value of integrating EBM alongside QMRA and QCRA. EBM provided evidence of mixture toxicity that complemented targeted chemical monitoring, and supported the interpretation of chemical risk by confirming that toxicological responses were consistent with the presence of THMs—particularly brominated species that, despite their lower concentrations, contributed more significantly to chemical DALYs. EBM was shown to be especially useful when toxicological parameters are incomplete or when mixtures of unknown or emerging compounds may be present. The coherence observed between chemical DALY estimates and bioassay responses strengthened confidence in the risk interpretation and highlighted the importance of using complementary lines of evidence in modern drinking water safety assessment.

A central outcome of the deliverable is the demonstration that DALYs represent a powerful harmonizing metric, allowing microbial and chemical risks to be expressed on the same scale and enabling explicit, quantitative evaluation of their trade-offs. This common metric makes it possible to compare health impacts objectively, regardless of hazard class, time horizon, or exposure mechanism. The DALY-based results consistently showed that microbial risks, when untreated, dominate the overall health burden, reinforcing the paramount importance of microbiological safety in water supply.



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Meanwhile, chemical risks, though generally smaller, must not be neglected—particularly in systems requiring higher disinfectant doses or experiencing network-related DBP formation.

Finally, the decision tree developed in this deliverable demonstrated that the integrated framework can adapt to a wide range of data availability scenarios—from high-resolution microbial time series (Berlin), to combined but moderate microbiological and chemical data (Ukraine), to full integration with EBM and advanced statistical modelling (Milan). This flexibility makes the framework suitable for both data-rich and data-limited contexts and aligns it with the operational diversity expected across European drinking water systems. By providing a structured, transparent, and scalable methodology, the integrated approach developed in D4.3 strengthens risk-based water management and supports SafeCREW's broader objective of enabling climate-resilient, health-protective drinking water systems.



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